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VEHICLES IN TOPICAL DERMATOLOGIC THERAPY

Their Functions and Physicochemical Characteristics

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I. INTRODUCTION

In the preparation of a dermatologic, therapeutic material for topical application, it is not uncommon for the vehicle to be given too little consideration. Custom too often determines the selection of the vehicle. Its choice may depend more on pleasing physical properties than on therapeutic efficacy. Such properties of a vehicle as odor, color, stability and compatibility with various drugs are emphasized. It is our belief that sufficient thought is rarely given to the functions which the vehicle performs or to such physicochemical characteristics of the vehicle as its ability to dissolve drugs, to cool the skin and to wet the skin.

In the literature, there are relatively few papers which correlate the various functions of vehicles with their physical and physicochemical properties or which discuss the physicochemical action of the vehicles on the skin. There is one German monograph on this subject by Czetsch-Lindenwald and Schmidt-LaBaume,[1] but no similar text in English has come to our attention. There has been considerable investigation of the action of specific drugs in various vehicles, such as the recent series of papers by Strakosch,[2] each of which contains a complete bibliography.

In the choice of a vehicle, one may need to consider: (1) the general characteristics of the patient's skin—e.g., whether it is oily, dry, light, dark, "thin" or "coarse"; (2) the area of skin being treated —e.g., whether it is hairy or glabrous; (3) the kind of lesions present—e.g., oozing or hyperkeratotic lesions; (4) the effect of the vehicle on the drug—e.g., hydrolysis, oxidation or chemical combination; (5) the effect of the drug on the vehicle—e.g., separation of an emulsion type of vehicle; (6) changes which occur in the vehicle after application to the skin—e.g., evaporation or oxidation; (7) influence of the vehicle on the action of the drug on the skin—e.g., increase in the penetration of the drug, and (8) action of the vehicle itself on the skin—e. g., prevention of evaporation or emollient action.

For the purpose of this discussion, a therapeutic material for topical application is considered to be a vehicle containing one or more drugs. There are four ways in which a therapeutic material may act when applied to the skin.

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1. Czetsch-Lindenwald, H., and Schmidt-LaBaume, F.: Salben und Salbengrundlagen, Berlin, Julius Springer, 1937.

2. Strakosch, E. A.: Studies on Ointments: I. Penetration of Various Ointment Bases, J. Pharmacol. & Exper. Therap. **78**:65-71 (May) 1943; II. Ointments Containing Salicylic Acid, Arch. Dermat. & Syph. **47**:16-26 (Jan.) 1943; III. Ointments Containing Sulfur, ibid. **47**:216-225 (Feb.) 1943; IV. Local Action of Salicylic Acid Plus Sulfur from Various Ointment Bases, ibid. **48**:384-392 (Oct.) 1943; V. Ointments Containing Resorcinol, ibid. **48**:393-399 (Oct.) 1943.

First, it may react chemically with the skin by such processes as direct chemical combination, oxidation or reduction. The exact chemical reactions of many drugs with the skin are not well understood, but much clinical experience has taught the physician how to use such substances as sulfur, salicylic acid, tar and boric acid. The vehicle, however, is not thought to undergo chemical reactions with the skin.

Secondly, if a drug penetrates the skin, it may directly alter the physiologic activity of the skin. If a specific alteration of a physiologic property of the skin is desired, however, it is more easily accomplished by ingestion or injection of the drug than by topical application (compare the action of pilocarpine when injected intramuscularly and when topically applied). The vehicle by itself seldom directly alters the physiology of the skin, but in so far as it may affect the penetration of the drug, it may indirectly influence the physiologic activity of the skin.

Thirdly, a topical application may cause an immune reaction to occur. There are few topical therapeutic procedures which depend on this type of reaction for their effectiveness. In fact, when such reactions do occur, as in the case of a contact dermatitis in which one of the topically applied substances is the allergen, it is an indication that such treatment should be stopped. When the therapeutic material is allergenic, either the drug or the vehicle may be the allergen, but rarely have immune reactions to vehicles been noted.

Fourthly, a topical application may produce a physicochemical effect. In fact, almost all therapeutic materials influence the skin in one way or another by virtue of their physical and physicochemical properties. A material which has a low boiling point will cool the skin when it evaporates; an occlusive covering will warm the skin by preventing normal evaporation of the sweat and retarding radiation of heat; an oily material will make the skin more "supple"; an oil solvent will make the skin more "brittle." The physicochemical action of a therapeutic material is more likely to be determined by the vehicle than by the drug.

Thus, in topical, dermatologic therapy, the vehicle rarely undergoes a specific biochemical reaction with the skin, and physiologic and immune reactions to the vehicle are relatively unimportant, but physicochemical changes do occur each time a therapeutic material is placed on the skin. These physicochemical actions, which depend primarily on the vehicle, may be an important part of the entire action of the complete therapeutic material.

This review will discuss these physicochemical characteristics of vehicles and the various functions which the vehicles perform. It is hoped that a better understanding of these principles will aid the physician in choosing the correct vehicle in topical, dermatologic therapy,

II. CLASSIFICATION OF VEHICLES

It is often difficult to decide just what constitutes a drug and what constitutes a vehicle in any therapeutic material. One might argue as to whether the starch in a paste or the zinc oxide in a shake lotion is a drug or a part of the vehicle. So far as is now known such powders do not react chemically with the skin and do not directly alter its physiologic activity. They do exert physicochemical actions on the skin. Perhaps no sharp line can be drawn between drugs and vehicles in all pharmaceutic preparations. For the purpose of this discussion, however, those materials which have a biochemical or physiologic action will be called drugs and those which are likely to affect the skin only physicochemically will be called vehicles.

In the following classification, this physicochemical action on the skin has been used to determine the position of the vehicle in the classification. We have chosen to classify the vehicles according to whether they act on the skin primarily as (*a*) an aqueous vehicle, (*b*) an oily vehicle, (*c*) a powder or (*d*) an organic solvent.

A. Vehicles which act as aqueous mixtures
   1. Water
   2. Shake lotions—e. g., a mixture of zinc oxide and water
   3. Gels of hydrophilic colloids—e.g., bentonite jelly or surgical lubricant

B. Vehicles which act as oils
   1. Water-immiscible oils—e. g., petrolatum or olive oil
   2. Water-miscible oils—e. g., anhydrous wool fat
   3. Oil in water emulsions—e. g., vanishing creams
   4. Water in oil emulsions—e. g., hydrous wool fat
   5. Pastes—e. g., a mixture of starch and petrolatum
   6. Collodions

C. Vehicles which act as powders
   1. Hydrophilic powders—e. g., starch
   2. Hydrophobic powders—e. g., talc or zinc stearate

D. Vehicles which act as organic solvents
   1. Water-miscible solvents—e. g., alcohol or acetone
   2. Water-immiscible solvents—e. g., ether

Physically, vehicles are liquid, semisolid (such as petrolatum) or solid. The preceding classification does not always distinguish between two vehicles of different states. For instance, olive oil and petrolatum would each be classified as a water-immiscible oil. Gels of hydrophilic colloids may be semisolid but nevertheless are classified as aqueous vehicles. The classification of many of those vehicles which are mixtures (emulsions, collodions) is determined not by the predominant characteristic of the vehicle as such, but rather by its characteristics after it has been on the skin for a while. An oil in water emulsion may contain 75 per cent water and have many of the characteristics

of water when it is applied to the skin, but soon after it is applied to the skin the water evaporates, and a film of water-miscible oil is left on the skin, after which the vehicle acts more like an oily vehicle than an aqueous one. A collodion often contains over 90 per cent of some organic solvent. After it is placed on the skin, however, this solvent evaporates, leaving behind a film of flexible collodion which will be shown to have many of the properties of a film of a water-immiscible oil. It is possible that both shake lotions and gels of hydrophilic colloids should be classified as powders rather than as aqueous vehicles, since a large part of the time they are on the skin they act more like powders than like aqueous mixtures.

III. PHYSICOCHEMICAL CHARACTERISTICS OF VEHICLES

For a better understanding of the functions of vehicles it is considered important first to review briefly some of the physical and physicochemical properties of vehicles.

A. Solubility of Drugs in Vehicles.—The solvent action of the vehicle is important from three points of view. The major consideration is the ability of the vehicle to dissolve the various drugs which are incorporated into it. Of less importance, no doubt, is the ability of the vehicle to dissolve secretions of the skin. Finally, in a few instances, consideration must be given to the solubility of substances which may come into contact with the vehicle from the environment after the vehicle has been applied to the skin.

A vehicle may carry a drug in true solution or in mechanical suspension. It is probable that no substance is completely insoluble in any vehicle, but some substances are so slightly soluble that they may be considered insoluble for purposes of this discussion, and when placed in a vehicle in which they are insoluble they will be held in that vehicle as a mechanical suspension. There are two major types of solvents among the vehicles—aqueous and oily. There are, of course, many types of oils used as vehicles. Solubility of the drugs in the oils will vary, but in general, drugs which are soluble in water are sparingly soluble in oils, and vice versa.

The solubility of some of the commonly used drugs in various solvents is shown in table 1. Solubility as a rule increases with the temperature. For the purpose of simplicity, the temperature factor is omitted from this table; all solubilities shown are for temperatures between 20 C. and 30 C., the approximate range for room and skin temperatures.

The ability of the vehicle to dissolve skin secretions and the protection the vehicle offers from air-borne substances need not be discussed here, since they will be considered as specific functions of the vehicle when applied to the skin.

TABLE 1.—*Solubility of Drugs in Various Vehicles*

Drug	Vehicle		
	Water	Ethyl Alcohol	Miscellaneous
Boric acid H_3BO_3	6.65 Gm./100 Gm. water *	6.85 Gm./100 cc. sol.†	Glycerine: 25 Gm./100 cc.‡
Potassium permanganate $KMnO_4$	9 Gm./100 Gm. water *	Decomposes ‡	
Sodium chloride NaCl	36 Gm./100 Gm. water *	0.4 Gm./100 Gm. alc.†	Glycerine: 10 Gm./100 cc.‡
Magnesium sulfate $MgSO_4.7H_2O$	81.4 Gm./100 Gm. water *	4.1 Gm./100 Gm. abs. alc.§	Glycerine: 91 Gm./100 cc.‡
Aluminum chloride $AlCl_3$	69.87 Gm./100 cc. water §	.....	Glycerine: soluble ‡
Calcium hydroxide $Ca(OH)_2$	0.15 Gm./100 Gm. water *	.....	Glycerine: 0.55 Gm./100 cc. 20% sol.†
Sodium perborate $NaBO_3.4H_2O$	3.78 Gm./100 cc. water §		
Zinc oxide ZnO	0.001 Gm./100 Gm. water §	Insoluble §	
Salicylic acid	0.25 Gm./100 Gm. sol.†	33.2 Gm./100 Gm. sol.†	Liquid paraffin: nil † Castor oil: 14.81 Gm./100 Gm.† Olive oil: 2.43 Gm./100 Gm.†
Benzoic acid	0.345 Gm./100 cc. sol.†	47 Gm./100 cc. alc.§	Castor oil: 14.7 Gm./100 Gm.† Olive oil: 3.96 Gm./100 Gm.† Glycerine: 9.07 Gm./100 Gm.†
Sulfur	Insoluble §	0.053 Gm./100 Gm. abs. alc.†	Wool fat: 0.38 Gm./100 Gm.† Olive oil: 1 Gm./100 cc.‡ Light oil: 0.324 Gm./100 Gm. sol.† Heptane: 0.362 Gm./100 Gm. sol.† Various coal tar oils: from 3 to 8.5 Gm/100 cc.† Saturated solution calcium hydroxide: 0.112 Gm./100 cc.†
Phenol	8.8 Gm./100 Gm. sol.†	Infinitely soluble §	Paraffin: 1.66 Gm./100 Gm.† Petrolatum: soluble ‡ Liquid petrolatum: soluble ‡ Glycerine: soluble ‡

* International Critical Tables, National Research Council, ed. 1, New York, McGraw-Hill Book Company, Inc., 1926-1930.
† Seidell, A.: Solubilities of Inorganic and Organic Compounds, ed. 3, New York, Van Nostrand Company, Inc., 1940, pt. 1; 1941, pt. 2.
‡ Wood, H. C., and Osol, A.: United States Dispensatory, ed. 23, Philadelphia, J. B. Lippincott Company, 1943.
§ Hodgman, C. D.: Handbook of Chemistry and Physics, ed. 27, Cleveland, Chemical Rubber Publishing Company, 1943-1944.

B. Heat of Vaporization.—When a liquid stands in an open container, some of the molecules of that liquid continuously escape from the liquid into the air. The rate of escape of these molecules into the air increases as the temperature is increased until the boiling point is reached. At any temperature less than either boiling point of two liquids, the liquid of the lower boiling point will volatilize at a faster rate than the liquid with the higher boiling point. This rate of evaporation is directly proportional to a property of the liquid called its vapor pressure, i. e., the higher the vapor pressure of a liquid, the more rapid will be its rate of evaporation.

If during the spontaneous evaporation of a liquid in an open container at a temperature below its boiling point the temperature of the liquid is taken at regular intervals, it will be found to decrease. During the process of evaporation heat will be absorbed from the container, and the temperature of the container will drop. This is the situation which exists when a liquid evaporates from the surface of the skin; the

TABLE 2.—*Cooling Effect of Various Vehicles*

Vehicle	(A) Vapor Pressure (Cm. of Mercury) 30 C.	(B) Molar Heat of Vaporization (Cal./G. Mol. Wt.) 30 C.	(A × B)	Approximate Relative Cooling Effect
Water	3.15	10,423	32,732	1.0
Ethyl alcohol	7.85	9,808	76,992	2.3
Acetone	28.10	7,547	212,070	6.5
Ether	63.48	6,312	400,686	12.2

temperature of the skin tends to drop and actually does drop unless heat is being supplied to the skin from the underlying tissues or from the surrounding environment at a rate equal to or exceeding the rate at which it is being lost as a result of evaporation and radiation from the surface. The amount of heat lost from the container (supplied to the liquid) when a molecular weight of a liquid evaporates is a property of the liquid and is called its molar heat of vaporization. The larger the molar heat of vaporization the greater the heat loss from the container when the liquid evaporates.

It is thus apparent that the cooling effect on the skin during the evaporation of a liquid will be dependent on the vapor pressure and the molar heat of vaporization of the liquid; roughly the cooling effect will be proportional to the product of these two factors. Table 2 shows the vapor pressure and molar heat of vaporization of some of the liquids sometimes placed on the skin and the approximate cooling effect of the liquids, taking the evaporation of water in dry air as unity.

Such substances as petrolatum also evaporate, but their vapor pressures are so low and their rates of evaporation consequently so slow

that they do not withdraw heat from the skin at a faster rate than it is supplied and therefore do not cool the skin. On the contrary, since they form a relatively occlusive film over the skin, they actually inhibit evaporation of the water normally given off by the skin and therefore have a "heating" effect on the skin.

C. Emulsions and Suspensions.—Vehicles may have a single phase or two phases. A phase is a homogeneous portion of matter which has uniform physical properties and which is separated from other phases by definite bounding surfaces.[3] A phase may be gaseous, liquid or solid, but gaseous phases will be given no consideration here, since no vehicle is used in dermatologic therapy in which a gas is one of the phases. The two phase vehicles which are used consist of either two liquid phases (emulsions) or a solid and a liquid phase (suspensions). Petrolatum and the semisolid fats should be thought of as liquids, since at the cutaneous temperatures at which they are used they have the properties of a liquid.

In a two phase system, one substance is dispersed as small particles in the second substance. The substance existing as distinct small particles is called the "dispersed" or "internal" phase; the second substance constitutes the "continuous" or "external" phase.

If two immiscible liquids such as oil and water are shaken together, one of the substances will be dispersed in the other. Soon after the shaking has stopped, however, the substances will again separate into two layers. Such a dispersion would be of little value as a vehicle. In order to be a satisfactory vehicle, a dispersion must be relatively permanent, i. e., it must show little change in its physical characteristics when it ages, when drugs are added to it or when it is subjected to changes in temperature and p_H (within limits).

In order to make a relatively permanent emulsion it is usually necessary to add a small quantity of a third substance to the two main constituents of the emulsion—the oil and the water. This third substance is called the emulsifying agent. The detailed theory of the action of emulsifying agents may be found in almost any textbook on physical or colloidal chemistry or in a book specifically covering this subject by Clayton.[4] The theory of emulsification will be discussed here in only brief and general terms.

When two immiscible liquids are stratified, there is a relatively small area of contact between them. When, however, one of these liquids is broken up into very small particles which are uniformly dispersed in

3. Getman, F. H., and Daniels, F.: Outlines of Physical Chemistry, ed. 7, New York, John Wiley & Sons, Inc., 1943.

4. Clayton, W.: Theory of Emulsions and Their Technical Treatment. Philadelphia, The Blakiston Company, 1943.

the second liquid, there is a great increase in the surface of contact. This results in a large increase in the surface energy, and the greater the surface energy, the more unstable is the dispersion. Decreasing the size of the particles of the dispersed phase only serves to increase the total surface energy. This surface energy is the product of the area and the surface tension between the two liquids at the surface of contact, i. e., the interfacial tension. An emulsifying agent is a substance which will reduce the interfacial tension and consequently the total surface energy and thus tend to stabilize the emulsion.

The size of the dispersed particles is dependent on the characteristics of the two phases and the emulsifying agent and also on the method used to prepare the emulsion. The diameter of the particles of the dispersed phase is usually from 10^{-4} mm. to 10^{-2} mm.

Two immiscible liquids can produce two types of emulsions; either of the liquids can be dispersed in the other. In most emulsions one of the liquids is water and the other is referred to as an oil. The types of emulsions are therefore oil in water and water in oil. In the first case, the oil is the dispersed phase and the water the continuous phase; in the water in oil emulsions, the water is the dispersed phase and the oil the continuous.

The type of emulsion produced is not determined primarily by the relative amounts of the two phases, but is determined by the type of emulsifying agent used. Some substances favor the production of oil in water emulsions; others favor the water in oil type. The important emulsifying agents used in vehicles, grouped according to the type of emulsion which results when they are used, are as follows: Emulsifying agents which favor the production of oil in water emulsions are (1) sodium, potassium and ammonium soaps; (2) sulfated oils, alcohols, esters, etc.; (3) mixtures of triethanolamine and fatty acids; (4) gums, such as acacia and tragacanth; (5) alkyl aromatic sulfonates, and (6) polyethers and polyalcohols.

Emulsifying agents which favor the production of water in oil emulsions are (1) sterols and sterol esters, such as wool fat; (2) calcium, zinc and aluminum soaps, and (3) fatty amides, secondary amides and alkylolamides.

Each of these emulsifying agents is characterized by the fact that a portion of its molecule is attracted to water (hydrophilic or polar group) and another part is attracted to the oil (lipophilic, hydrophobic or nonpolar group). The important hydrophilic groups are -COOH, -COONa, $-SO_3Na$, $-OSO_3Na$; the lipophilic group is usually a long chain hydrocarbon.

One may wish to determine whether a certain vehicle is an emulsion and if so, what type it is. This is not always easy to do, but some of the simpler tests will be given. When the refractive indexes of its

two phases differ, as is usually the case, an emulsion is likely to be more opaque than either of its phases (compare cold cream and mineral oil). A relatively clear material may be an emulsion, but if so it will show a Tyndall effect (scattering a beam of light by the dispersed particles of the emulsion). Once it is determined that the vehicle is an emulsion, its type can usually be determined by one or more of three simple tests:

1. If a water-soluble dye dissolves easily in the emulsion without agitation, the emulsion is the oil in water type; if an oil-soluble dye dissolves easily, it is the water in oil type.

2. If an emulsion is easily diluted with water without changing the characteristics of the emulsion, it is an oil in water emulsion; if it dilutes with oil, it is water in oil.

3. If it is a good conductor of electricity, it is an oil in water emulsion.

It has been stated that it is important that an emulsion which is to serve as a vehicle remain stable. And yet in the case of most emulsions, there is a tendency for the particles of the dispersed phase to coalesce, thus tending to cause the emulsion to separate into two layers (creaming or breaking). Certain factors tend to accelerate the rate at which emulsions break, and unfortunately the addition of certain drugs causes many emulsion type vehicles to break. Some of the classes of substances which cause emulsions to break are: (1) those substances which appreciably change the p_H of an emulsion, (2) soluble inorganic salts of polyvalent ions and (3) powders. Some apparently stable emulsions, which might be expected to be good vehicles, break so easily on the addition of certain drugs that they are unsatisfactory vehicles.

If the dispersed phase is a solid and the continuous phase is a liquid, the resultant two phase system is called a suspension. Shake lotions and pastes are examples of such two phase systems. In the commonly used vehicles, the particles of the solid phase are relatively large, and the resultant suspensions are unstable. The solid phase quickly settles when the continuous phase is a liquid of low viscosity, such as water. When the continuous phase is a semisolid material of high viscosity, such as the petrolatum of a paste, the solid phase remains suspended for some time.

In a suspension in which the solid particles are small enough to be colloidal (from 1 to 100 millimicrons), the suspension is relatively stable. When the continuous phase is water, the dispersed phase may be either hydrophobic or hydrophilic. Only the latter type of colloidal suspensions will be discussed here. In this group belong starch, gums and the recently developed colloidal clays or bentonites.

Mixtures of these materials with water vary widely in their physical characteristics. They may be similar to water, such as a starch bath,

or they may have a semisolid consistency, such as a bentonite gel. The characteristics of these suspensions are dependent on such factors as the concentration of the dispersed phase, the method of preparation and the temperature of the supension.

Many of the hydrophilic colloid preparations are liquid at elevated temperatures (sols) and have a semisolid consistency at lower temperatures (gels). This phenomenon is often experienced in solutions of agar, gelatin or gum. Some of the gels of the hydrophilic colloids so resemble petrolatum that a physician is apt to use them as petrolatum would be used. It should not be forgotten, however, that a large part of the volume of these gels is water and that, therefore, these gels more closely resemble the shake lotions than they do the ointments or pastes so far as their use in dermatologic therapy is concerned.

In smaller amounts, the hydrophilic colloids serve as emulsifying and suspending agents. The gums were included in the foregoing list of emulsifying agents and were seen to favor the production of oil in water emulsions. Colloidal clays have been found to serve as emulsifying agents for both types of emulsions. The addition of a little bentonite to a suspension of zinc oxide causes the particles to stay suspended for a much longer time.

The physical state of the vehicle, that is true solution, emulsion or suspension, will be shown to have an important bearing on the functions of vehicles used in dermatologic therapy.

D. Theory of Wetting Action.—Few fields of physical chemistry have developed as rapidly during the past two decades as that pertaining to the wetting or surface-active agents. Only recently have these substances been used by the medical profession, and Duemling [5] made the first comprehensive report known to us of their use in vehicles for dermatologic topical therapy. Many of the recently prepared emulsion type ointment bases contain wetting agents as emulsifiers. In many respects, the wetting agents resemble the new detergents, which have been discussed by us.[6]

When a liquid or semisolid substance is placed on the skin, a new junction (more correctly called "interface") is formed, i. e., the skin-air interface is replaced by a skin-liquid interface. This phenomenon of a liquid coming into contact with a solid to form a solid-liquid interface is termed "wetting" and those substances which, when added to

5. Duemling, W. W.: Wetting Agents: New Synthetic Chemicals of Use in Finer and More Efficient Topical Dermatologic Therapy, Arch. Dermat. & Syph. **43**:264-280 (Feb.) 1941.

6. Lane, C. G., and Blank, I. H.: Cutaneous Detergents Other Than Soap, in A Symposium on Medical Uses of Soap, Philadelphia, J. B. Lippincott Company, 1945.

the liquid, aid in establishing this contact are called "wetting agents" or "surface-active agents." Wetting agents may also, of course, aid in establishing contact between two immiscible liquids, in which case the wetting agents are as a rule good emulsifying agents, which have already been discussed. Many papers have been published on the physical chemistry of wetting. Those interested in the detailed physicochemical aspects of this subject should consult a series of papers by Bartell and his co-workers [7] and the accompanying bibliographies.

Three types of wetting are possible: adhesional, spreading and immersional. For a consideration of the contact of various vehicles with the skin, only spreading wetting is important. Immersional wetting is important, however, in the incorporation of some medicaments into vehicles, particularly the solids into the liquid vehicles.

Whether or not a liquid will tend to spread over a solid surface is dependent on the free surface energies involved. When a liquid spreads, a solid-air interface is replaced by a solid-liquid interface and a liquid-air interface. If the sum of the free surface energies of these two new interfaces is less than the free surface energy of the original solid-air interface, then the liquid will tend to spread; if it is greater, the liquid will not spread. Up to now there has been no method devised for measuring these free surface energies, since the interfacial tension cannot be measured when one of the surfaces is a solid. The interfacial tension is, however, a function of the contact angle which the liquid makes with the solid. The contact angle is the angle between the surface and the tangent to the liquid surface at the point of contact with the solid, measured through the liquid. Various methods have been devised for measuring the contact angle. The smaller the contact angle, the more easily a liquid spreads over a solid surface. Spontaneous, complete spreading takes place only when the contact angle is zero. Numerous difficulties arise when an attempt is made to measure the contact angle between a liquid and an uneven, nonhomogeneous surface, such as the cutaneous surface. To our knowledge, such a measurement has not yet been successsfully made.

The ability of a vehicle to wet the skin plays an important role in the action of the vehicle on the skin, and this characteristic will be further considered in the discussion of various functions of the vehicle.

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7. Bartell, F. E.: Wetting of Solids by Liquids, in Alexander, J.: Colloid Chemistry, New York, Chemical Catalogue Company, 1931, vol. 3, pp. 41-60. Bartell, F. E., and Wooley, A. D.: Solid-Liquid-Air Contact Angles and Their Dependence upon the Surface Conditions of the Solid, J. Am. Chem. Soc. **55**:3518-3527 (Sept.) 1933. Bartell, F. E., and Bartell, L. S.: Quantitative Correlation of Interfacial Free Surface Energies, ibid. **56**:2205-2210 (Sept.) 1934. Bartell, F. E.: Wetting Agents, Indust. & Engin. Chem. **33**:737-740 (June) 1941.

IV. FUNCTIONS OF VEHICLES

A vehicle has many functions to perform. The more important of these functions are as follows:

A. It carries a drug to the skin and holds it there.

B. It influences the penetration of a drug into and through the skin.

C. It alters evaporation from the cutaneous surface.

D. It alters the texture of the skin.

E. It protects the skin.

F. It aids in the removal of cutaneous secretions. Each of these functions will be discussed for the various classes of vehicles.

A. Carrier for a Drug.—This function is probably the most important function of the vehicle. Seldom are drugs applied directly to the skin. They are first dispersed in the vehicle, and it is the function of the vehicle to distribute the drug over the diseased surface of the skin and to hold it there to produce the desired effect. In choosing the vehicle to perform this function, it is necessary to consider three physicochemical characteristics of the vehicle, which are: (1) the solvent action of the vehicle for the drug, (2) the volatility of the vehicle and (3) the ability of the vehicle to permit transfer of the drug from the vehicle to the skin.

1. Solubility of the Drug in the Vehicle: A vehicle may carry a drug in solution or in suspension. When the drug is present in true solution, its state of subdivision is molecular or smaller than molecular. In colloidal solutions of drugs, the particle size is very small but it is larger than molecular. In suspensions, the particle size of the drug is still larger, and its size will be determined by the method used to produce the suspension. The most uniform distribution of the drug over the surface of the skin is accomplished when the drug is in true solution in the vehicle.

In true solutions and in colloidal solutions the drug moves about freely in the vehicle. If the drug is present in suspension, the particles are too large to move and remain in a fixed position. Theoretically, therefore, when a drug is applied to the skin in a vehicle in which it is soluble, the entire amount of the drug is available to the skin. That is to say, those molecules of the drug which are not at the interface between the vehicle and the skin when the therapeutic material is first applied to the skin will reach the interface at some later time because they move about freely in the solution. When the drug is present in suspension, however, only those particles of the drug which are at the interface when the material is applied will come into contact with the skin. The particles at a distance from the interface cannot move about and are not available to the skin. It would be expected, therefore, that

when salicylic acid is applied to the skin in castor oil, in which it is soluble, much more of the salicylic acid would be available to the skin than when it is applied in petrolatum, in which it is insoluble.

When the concentration of a drug which is soluble in a given vehicle is increased within the limits of its solubility, it may be theoretically assumed that the action of that drug on the skin will be increased in direct proportion to the increase in concentration. Consider the example in which the concentration of the drug is doubled. The number of molecules of the drug originally in contact with the skin will be doubled, and the number reaching the skin as the molecules move about will likewise be doubled. The action on the skin should therefore also be doubled.

When the concentration of a drug which is insoluble in a given vehicle is increased, the action of the drug on the skin may not be increased in direct proportion to the increase in concentration. When the concentration is doubled, the amount of drug in contact with the skin when first applied will be doubled, but if some of this is used up by reaction with the skin, no more will be brought to the surface of the skin, since the suspended particles do not move about in the vehicle. Therefore, a 2 per cent solution of salicylic acid in castor oil might be expected to have twice the effect on the skin of a 1 per cent solution, but it does not follow that a 2 per cent suspension of salicylic acid in petrolatum will have twice the effect of a 1 per cent suspension.

This last example of an insoluble drug in a nonvolatile, oily vehicle represents the type of therapeutic material most commonly used in the treatment of diseases of the skin. Petrolatum is a frequently used vehicle, and most drugs are relatively insoluble in it. In doubling the concentration of a drug in petrolatum, a physician often feels that he has prescribed an ointment which is twice as strong as a previously prescribed ointment. Strakosch [2] showed that the keratolytic action of salicylic acid in petrolatum is increased by increasing the concentration of the salicylic acid, but that the rate of keratolytic action is not increased in direct proportion to the change in concentration of the salicylic acid. Abramowitz [8] found that some ointments containing large amounts of sulfur were apparently milder than ointments containing less sulfur.

2. Volatility of the Vehicle: When a large volume of a therapeutic material made with a volatile vehicle is used for a short time only, evaporation of the vehicle does not alter the action of the therapeutic material on the skin. The small amount of evaporation which takes place when an extremity is soaked for a short time in a large volume

8. Abramowitz, E. W.: External Use of 30 to 50 Per Cent Sulfur in Petrolatum in Various Dermatoses, New York State J. Med. **43**:746-753 (April 15) 1943.

of boric acid solution or when a potassium permanganate bath is taken changes the action of these solutions little because the concentration of the drug is only slightly increased. When only a small volume of such a therapeutic material is used, however, the evaporation of the vehicle may definitely alter the action of the material on the skin.

The entire vehicle may be volatile, such as ethyl alcohol, or only part of the vehicle may be volatile, such as emulsions or collodions. When the entire vehicle is volatile, the drug which it contains will be deposited on the skin "in 100 per cent concentration" after the vehicle evaporates, independent of the original concentration of the drug in the therapeutic material. When the vehicle is as volatile as alcohol, the concentration rapidly changes after the therapeutic material is applied to the skin. Stronger tincture of iodine (7 per cent) will deposit three and one-half times as much iodine on the skin as will mild tincture of iodine (2 per cent) when equal volumes of the two solutions are placed on equal areas of the skin. Any greater reaction which may result from the application of stronger tincture of iodine will be caused not by the action of the 7 per cent iodine solution as such but by the greater amount of iodine deposited on the skin when the vehicle evaporates.

When a vehicle a portion of which is easily volatile is prescribed, it must be remembered that the characteristics of the therapeutic material and the concentration of the drug as specified by the physician are changed subsequent to the evaporation of the volatile part of the vehicle. When an oil in water emulsion, such as a vanishing cream, is used as a vehicle, the water phase quickly evaporates, leaving a film of a water-miscible oil with the drug probably in suspension. The original advantage of having the drug in solution (if the drug is water soluble) disappears when the water evaporates. Likewise when a vehicle is a shake lotion or a gel of a hydrophilic colloid, the evaporation of the water leaves the drug on the skin mechanically mixed with a hydrophobic or hydrophilic powder (for the shake lotion) and with a hydrophilic film (for the colloidal gel). In the case of collodions, a large percentage of the drug may be made inactive when it is encased in a hydrophobic film after the evaporation of the solvent.

3. Transfer of the Drug from the Vehicle to the Skin: Before a drug can exert a true chemical or physiologic action on the skin, it must be transferred from the vehicle which has served as its carrier to the skin itself. Also, chemical and physiologic reactions in the skin probably take place in an aqueous environment. Therefore, if a drug should be transferred from the vehicle to the oily film of the skin, such as the sebum, it must be further transferred to an aqueous fluid, such as perspiration or serous exudate. The skin, of course, contains large amounts of water and is continually giving off water as insensible and

sensible perspiration, which may accumulate on the cutaneous surface or in the cutaneous tissue if normal evaporation is inhibited by the vehicle. In some cutaneous lesions the surface is wet by serous exudate; in other lesions and in normal skin, oily sebaceous secretions probably constitute the surface film. The transfer of the drug from the vehicle to the skin will depend on the miscibility of the vehicle with the substances on the cutaneous surface and on the relative solubility of the drug in the vehicle and the cutaneous fluids.

A vehicle will be completely miscible only with a skin secretion or exudate which has characteristics similar to those of the vehicle. For instance, an aqueous vehicle will mix easily and completely with a serous exudate or with sweat but will not mix easily with an oily secretion such as the fatty film on the surface of normal unbroken skin. A hydrophobic oily vehicle, such as petrolatum, on the other hand, will mix with the fatty film but will not mix with sweat or with a serous exudate. A hydrophilic oily vehicle, such as wool fat, may be able to mix with both oily and aqueous surface films. Drugs in solution in aqueous vehicles will be easily transferred to aqueous cutaneous secretions or exudates; drugs which are readily soluble in oily vehicles will be easily transferred to oily cutaneous secretions.

The transfer of a drug dissolved in a vehicle to a cutaneous fluid with which the vehicle is not miscible may occur and will depend on the relative solubility of the drug in the vehicle and in the cutaneous fluid. A solute will distribute itself between two immiscible solvents in direct proportion to its relative solubility in the two solvents. Salicylic acid is six times more soluble in castor oil than in olive oil. Since it is much more soluble in either oil than in water, however, the amount of salicylic acid which will be transferred to water (and probably to aqueous cutaneous fluids) from a saturated castor oil solution will be little more than the amount that will be transferred from a saturated olive oil solution. The total reserve salicylic acid will, of course, be much greater in the castor oil solution.

A drug suspended in a vehicle may be dissolved out of the vehicle by a cutaneous fluid or secretion. This would be a type of leaching process. That is to say, salicylic acid may be leached from petrolatum in which it is suspended, by the aqueous cutaneous fluids, if these fluids can get in contact with the salicylic acid crystals. Probably, however, these crystals are coated with a film of petrolatum, and it is therefore difficult for water to come in contact with the crystals. The mechanism by which a salicylic acid crystal completely coated with petrolatum can become available to the aqueous fluids of the skin is not apparent to us. Possibly the salicylic acid is transferred to the more hydrophilic sebum from the petrolatum and can then be transferred to the aqueous fluids.

4. Summary: (*a*) When a vehicle carries a drug in true solution the drug will be distributed more uniformly over the surface of the skin than when the vehicle carries the drug in suspension.

(*b*) The action of a drug on the skin is more likely to vary in direct proportion to its concentration if a vehicle is used in which the drug is soluble than if one is used in which the drug is insoluble.

(*c*) When a volatile vehicle evaporates, the concentration of the drug changes and the means by which the drug is held on the skin is altered.

(*d*) A drug will be transferred most easily to the skin if the vehicle in which it is dissolved is similar to the cutaneous secretion or exudate with which it comes in contact.

(*e*) Transfer of a drug from a vehicle to a cutaneous fluid with which the vehicle is not miscible will depend on the relative solubility of the drug in the vehicle and in the cutaneous fluid.

(To Be Continued)

DERMATITIS FROM A LARGE DOSE OF PENICILLIN TAKEN ORALLY

Report of a Case

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IT IS not infrequent to find sensitivity to penicillin in persons who come in contact with it or who have received it intramuscularly or intravenously. No report has been found in the literature describing this reaction after oral administration. Penicillin is described as a drug having practically no toxicity and of which extremely large doses are tolerated for long periods of time without ill effects.

Lyons [1] reported an urticarial reaction in 12 out of 209 patients receiving penicillin therapy. Pyle and Rattner [2] recorded a case of dermatitis venenata of face and genitalia in a physician who came in contact with penicillin while preparing solutions and administering them to patients. Three of his orderlies handling penicillin also experienced slight itching, though no dermatitis developed. Binkley and Brockmole [3] reported 2 cases of contact dermatitis in which there was a focus of dermatophytosis pedis on the webs of the toes. Barker [4] reported 2 cases in which cutaneous lesions developed after clinical use. Criep [5] discussed a case of acquired sensitivity to penicillin in which he believes the allergy to be unrelated to penicillin spores, but to be analogous to drug or serum allergy. Feinberg [6] stated that the penicillin reaction does not resemble the classical and severe allergic reactions which would be likely to follow the injection of an allergen to which the person

From the Department of Biochemistry, The Wm. S. Merrell Co. (Dr. Oberst) and the Department of Physiology, University of Cincinnati (Dr. Murray).

1. Lyons, C.: Penicillin Therapy of Surgical Infections in the U. S. Army, J. A. M. A. **123**:1007-1018 (Dec. 18) 1943.

2. Pyle, H. D., and Rattner, H.: Contact Dermatitis from Penicillin, J. A. M. A. **125**:903 (July 29) 1944.

3. Binkley, G. W., and Brockmole, A.: Dermatitis from Penicillin, Arch. Dermat. & Syph. **50**:326-327 (Nov.) 1944.

4. Barker, A. N.: Allergic Reactions to Penicillin, Lancet **1**:177-178, 1945.

5. Criep, L. H.: Allergy to Penicillin, J. A. M. A. **126**:429-430 (Oct. 14) 1944.

6. Feinberg, S. M.: Penicillin Allergy, J. Allergy **15**:271-273, 1944.

has been naturally sensitive. He showed that when a fairly pure preparation of penicillin (630 units per milligram or greater) was administered no reaction was obtained in a penicillium-sensitive patient after a dose of at least 500,000 units.

During the course of a study on urinary excretion and blood levels of penicillin after oral and intravenous administration of penicillin,[7] one of us (F. W. O.) who served as a subject reacted severely to 50,000 units given intravenously. Within an hour he showed a dermatitis which after several hours became severe. The face reddened, small areas of erythema appeared all over the chest, and some swelling and small blisters appeared around the toes. The scalp and toes itched considerably at times. This general condition lasted for about three days.

Several weeks later the same dose of penicillin was taken orally with no noticeable reaction appearing. Repeated administrations at biweekly intervals of this size dose with and without food and with and without antacids were made at least ten times without producing a reaction at any time. However, when the dose was increased to approximately 500,000 units, a severe dermatitis resulted similar to the one from the 50,000 unit dose given intravenously. The penicillin used was suspended in oil and beeswax, put in soft gelatin capsules, and had a purity of 842 units per milligram.

About two hours after the oral dose there was itching of the toes, which were severely swollen about ten hours later. Numerous small blisters appeared in the web, followed by some oozing and lesions. By the third day small patches of epidermis peeled off where the lesions occurred. There was also a mild dermatitis on the chest, in the groin and under the chin, with some swelling and reddening around the eyes. The person had no history of eczema and had not previously experienced any allergic reactions. There was no evidence of fungous infection which might render him sensitive to a mold product occurring as an impurity in the product.

The mechanism for this condition is not clear, as other persons taking the same dose did not have dermatitis. It generally is believed that the reaction is not due to the penicillin per se but to impurities associated with it. By giving penicillin orally it was hoped that the chances of producing a dermatitis might be considerably decreased, unless the substance responsible for the reaction is absorbed from the

7. Oberst, F. W.; Nielsen, F. A., and Foter, M. J.: Blood Levels and Urinary Excretion of Penicillin After Oral Administration, Cincinnati J. Med., October 1946, to be published.

gastrointestinal tract. The dose used here was approximately ten times that given intravenously. Some authorities [8] state that it requires about five to ten times as much penicillin when given orally as when given intravenously or intramuscularly to obtain the same clinical effect. After the oral dose in this case there was undoubtedly about the same effective penicillin concentration in blood and tissues as after the 50,000 unit dose given intravenously.

8. Keefer, C. S.: Status of Oral Penicillin, J. Am. Pharm. A. (Pract. Pharm. Ed.) **6**:210, 1945.

CONTACT DERMATITIS FROM PENICILLIN

The Source of the Antigen

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ALLERGY to penicillin has been the subject of many recent reports. Various types of reactions are recorded which may be classified under the heading of hypersensitivity. The most common allergic response described is urticaria.[1] In most instances this resembles a serum sickness type of reaction and does not interfere with the continuation of treatment. In a few cases, more severe reactions have necessitated prompt cessation of therapy. Another type of reaction is a vesicular or bullous eruption occurring shortly after the onset of treatment, which appears to be in some manner related to a previous fungous infection of the skin.[2] Contact dermatitis is a third manifestation fre-

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The materials used in this study were supplied by the Abbott Laboratories, North Chicago, Ill.

From the Division of Allergy, Department of Medicine, Northwestern University School of Medicine, and the Plant Physician's Department of Abbott Laboratories.

1. Keefer, C. S.; Blake, F. G.; Marshall, E. K., Jr.; Lockwood, J. S., and Wood, W. J. Jr.; Penicillin in the Treatment of Infections: A Report of Five Hundred Cases, J. A. M. A. **122**:1217-1224 (Aug. 28) 1943. Lyons, C.: Penicillin Therapy of Surgical Infections in the U. S. Army, ibid. **123**:1007-1018 (Dec. 18) 1943. Criep, L. H.: Allergy to Penicillin, ibid. **126**:429-430 (Oct. 14) 1944. Price, D. E.; McNairy, D. J., and White, E. L.: Severe Asthma: Delayed Sensitization to Penicillin, ibid. **128**:183 (May 19) 1945. Sullens, W. E.: Simulating Serum Sickness Reaction to Penicillin, U. S. Nav. M. Bull. **45**:752-754 (Oct.) 1945.

2. Graves, W. N.; Carpenter, C. C., and Unangst, R. W.: Recurrent Vesicular Eruptions Appearing During Administration of Penicillin, Arch. Dermat. & Syph. **50**:6-7 (July) 1944. Cohen, M. T., and Pfaff, R. O.: Penicillin in Dermatologic Therapy: Report of Results of One Hundred Cases, ibid. **51**:172-177 (March) 1945. Binkley, G. W., and Brockmole, A.: Dermatitis from Penicillin: Report of Two Cases, ibid. **50**:326-327 (Nov.) 1944. Morris, G. E., and Downing, J. G.: Bullous Dermatitis (Dermatitis Medicamentosa) from Penicillin, J. A. M. A. **127**: 711 (March 24) 1945. Lamb, J. H.: Allergic Reactions During the Administration of Penicillin, Arch. Dermat. & Syph. **52**:93-95 (Aug.) 1945.

quently attributed to penicillin.[3] In addition to these three types of allergy, which comprise the majority of the reactions reported, a tuberculin type of response following a single intradermal injection,[4] and reactions of the Arthus type following repeated intradermal injections have been noted.[5]

Since the penicillin in common use contains a fair amount of impurities, doubt has arisen that the allergic reactions observed are caused by the active principle of penicillin itself. In a recent review of the subject, one of us (S.M.F.) [6] pointed out that the majority of reports lack in some respect the details necessary to provide a complete picture of the source and mechanism of allergy to penicillin. It is quite possible that more than one antigen accounts for the varied allergic reactions already noted. A more thorough study of patients presenting allergic symptoms from penicillin is necessary to determine the source and mechanism of such reactions.

We have recently encountered 5 cases of contact dermatitis in persons handling penicillin. All of the patients were completely relieved of symptoms when removed from contact with the drug. Four of these patients were industrial workers engaged in the manufacture of penicillin for commercial use, and 1 was a chemist producing the drug by the surface culture method for experimental study. We availed ourselves of the opportunity of determining the source of the allergen in these cases by making patch tests with substances entering into the manufacture of penicillin, the commercial penicillin salts and a chemically pure preparation of crystalline penicillin G. In addition, intradermal tests were carried out with mold extracts to determine any relationship that might exist between contact dermatitis and clinical allergy to molds. Four of the patients were available for testing at the time this study was made.

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3. (*a*) Pyle, H. D., and Rattner, H.: Contact Dermatitis from Penicillin, J. A. M. A. **125**:903 (July 29) 1944. (*b*) Silvers, S. H.: Contact Dermatitis from Amorphous Sodium Penicillin, Arch. Dermat. & Syph. **50**:328-329 (Nov.) 1944. (*c*) Barker, A. N.: Allergic Reactions to Penicillin, Lancet **1**:177-178 (Feb. 10) 1945. (*d*) Hanson, P. S.: Contact Dermatitis Caused by Commercial Penicillin: A Case Report, M. Bull. North African Theat. Op. **2**:118 (Nov.) 1944. Nelson, L. M., and Sandt, K. E.: Contact Dermatitis of the Eyelids as Result of Penicillin, ibid. **2**:62 (Sept.) 1944. Michie, W., and Bailie, H. W. C.: A Case of Penicillin Reaction, Brit. M. J. **1**:554 (April 21) 1945. Selinger, E.: Dermatitis of the Lids from Penicillin Eye Drops, J. A. M. A. **128**:437 (June 9) 1945.

4. Welch, H., and Rostenberg, A., Jr.: Hypersensitivity of Tuberculin Type to Crystalline Penicillin Sodium, J. A. M. A. **126**:10-12 (Sept. 2) 1944.

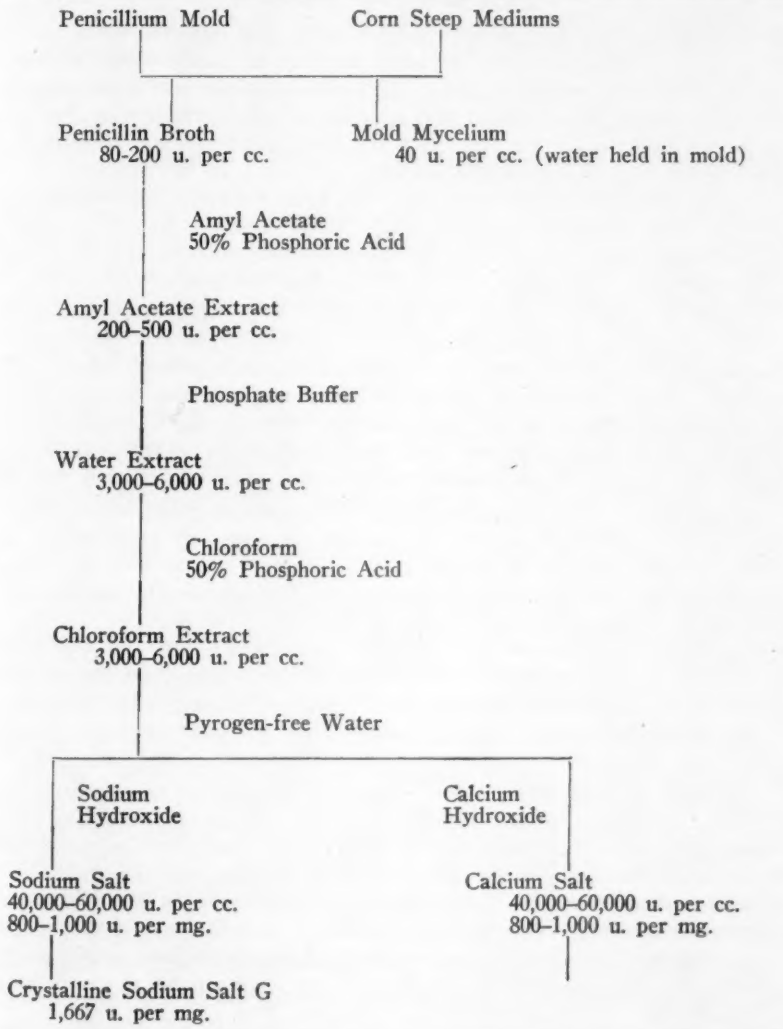
5. Rostenberg, A., Jr.: Local Penicillin Therapy, Arch. Dermat. & Syph. **50**:330 (Nov.) 1944.

6. Feinberg, S. M.: Allergy to Penicillin, J. Allergy **16**:302 (Nov.) 1945.

PRODUCTION OF PENICILLIN [7]

Most commercial preparations of penicillin are produced by the submerged broth method. A strain of Penicillium chrysogenum is grown in a corn steep liquor containing lactose and mineral salts. After adequate growth the mold mycelium is separated from the broth and extracted with solvents, such as amyl acetate and choloroform, finally ending up as the sodium or calcium salt of penicillin.

The Production of Penicillin



7. Sylvester, J. C.: Personal communication to the author.

The final solution is lyophilized to produce a powder containing approximately 60 to 70 per cent of penicillin. Approximately 90 per cent of the sodium or calcium salt is penicillin G. The crystalline sodium salt G is produced from commercial penicillin and is chemically pure (diagram). The surface culture method is not as well adapted for quantity production. A strain of Penicillium notatum is generally used, and the penicillin obtained contains appreciable amounts of penicillin X in addition to penicillin G.

REPORT OF CASES

CASE 1.—V. J., a 30 year old married woman, was employed in the penicillin department on May 26, 1944. Her work consisted of placing muslin covers over aluminum trays containing penicillin which had previously been frozen and dried to form a powder. On March 3, 1945 a pruritic eruption developed on the dorsum of the left hand and on the right wrist. A boric acid cream was prescribed, and the eruption improved for a time but recurred later. On two occasions she was away from work for periods of ten days and noted a decided improvement of the eruption, with recurrence on her return to work. On May 2, 1945 the eruption became aggravated, and in addition itching of the neck and eyelids developed. The patient was then transferred to another department, where all contact with penicillin was avoided. The dermatitis gradually cleared and has not recurred.

CASE 2.—J. M., a 56 year old man, was employed in the penicillin department on Jan. 12, 1944 and engaged in the extraction processes. On March 9, 1945 a pruritic eruption developed on the dorsa of the hands and forearms, with a diffuse maculopapular eruption on the face, forehead and neck. Local therapy failed to produce improvement. He was then removed from the penicillin division, and rapid disappearance of the eruption was observed without subsequent recurrence.

CASE 3.—J. R., a 33 year old man, was employed in the penicillin department on Oct. 14, 1943. His work consisted of the final extraction and purification of penicillin. Approximately four months later a pruritic vesicular eruption developed on the lateral and dorsal aspects of both hands. Hydrous wool fat and ointment of benzoic and salicylic acid were applied without relief. The wearing of cotton and rubber gloves failed to cause any improvement. He was seen on Oct. 24, 1945 with a vesicular scaly eruption on the fingers and hands and a diffuse eruption on the flexor surface of the right forearm. A sulfonated oil was prescribed, and soap and water were avoided for a period. As there was no improvement he was transferred from the penicillin department, after which the eruption disappeared.

CASE 4.—H. L. a white married woman, 52 years of age was employed in the penicillin department on Jan. 5, 1944. Her work consisted of inoculating the corn steep liquor with a suspension of Penicillium mold. Some time before November a dermatitis developed on the dorsal aspects of the hands and fingers. This was treated with cod liver oil and boric acid ointments, without improvement. She continued to work in the penicillin department until March 9, 1945, when an exacerbation of the dermatitis occurred on the forearms and face, as well as on the hands. She was then removed from her job, and the eruption was completely gone by March 23.

CASE 5.—C. F., a chemist aged 58, began producing penicillin by the surface culture method in September 1943. On March 3, 1945 a burning and itching of the eyelids developed and an eczematoid weeping eruption appeared on the skin of the

orbital regions. He discontinued work and was given several roentgen ray treatments to the involved areas, with gradual disappearance of the eruption. On April 8 he had a slight sore throat, and as a prophylactic measure he sprayed his throat with a penicillin solution containing 8,000 units per cubic centimeter. Shortly afterward he again noted itching of the eyelids with subsequent reappearance of the eruption, as well as itching and edema of the soft palate, uvula, and pharynx. Avoidance of penicillin resulted in prompt disappearance of symptoms. Later he tried taking penicillin in the form of a lozenge by mouth. This was followed in a few moments by itching and inflammation of the pharynx.

TESTING AND RESULTS

Individual patch tests were made on the back or on the lateral aspect of the arm. To insure potency, the substances used were obtained from a routine production run a few moments before their application. The patches were removed and the reactions noted at forty-eight hours, and a final reading was made at seventy-two hours.

Results of Test

	V. J.	J. M.	J. R.	C. F.
Penicillium mold	0	0	0	+
Corn steep liquor mediums	0	0	0	0
Mold mycelium (submerged culture) water held in mold containing 40 u./cc.	++	++	+	
Mold pellicle (surface culture)	..	..	..	+
Penicillin broth, 200 u./cc.	++	0	0	+
Amyl acetate extract, 300 u./cc.	+	0	0	
Water extract, 5,000 u./cc.	+++	+	0	
Chloroform extract, 3,000 u./cc.	++	+	+++	
Sodium salt of penicillin, 50,000 u./cc.	++	+	0	++
Calcium salt of penicillin, 50,000 u./cc.	++	+	0	
Crystalline sodium penicillin G, 8,000 u./cc.	+++	+	0	+++
Penicillium notatum 1:1,000 (intracutaneously), alternaria 1:1,000	0	0	0	0

+, slight; ++, moderate; +++, strong.

Intradermal tests with mold extracts were made on the forearm. Readings were made at fifteen minutes and at forty-eight and seventy-two hours. The results are summarized in the table.

Reactions to pure crystalline penicillin as well as to intermediary products were noted in 3 of the cases studied. These were significant in that tests on control subjects elicited negative reactions. In 1 patient (C. F.) a reaction occurred to the Penicillium mold, indicating that at least a small amount of the active principle of penicillin is contained in the original mold itself. Another patient (J. R.) failed to show reactions to the crystalline or the commercial preparations. A strong reaction to the chloroform extract was obtained, and a lesser reaction to the mold mycelium containing relatively little penicillin. At an earlier date, this subject was reported to have given a positive reaction to a patch test with dry penicillin powder containing 1,000 units per milligram. It is likely that the dermatitis observed in this patient was due to substances other than penicillin. Control tests with the mold mycelium

elicited negative reactions. The corn steep liquor medium failed to cause a reaction in any subject. No reactions, either immediate or delayed, occurred to the intradermal injections of mold extracts.

COMMENT

The rapidly increasing use of penicillin locally in such forms as ointments, sprays, drops, troches and lozenges will create many opportunities favoring the development of the contact type of allergic reaction. It is therefore of importance to recognize the potentialities of penicillin as a skin-sensitizing agent and to determine the active principle responsible for such reactions. Some attempt to locate the responsible factor has been made in previous reports. Pyle and Ratner [3a] described a case of contact dermatitis. The patient was a physician handling penicillin in whom patch tests with the commercial preparation and with the purest crystalline material then available elicited positive reactions. Silvers,[3b] on the other hand, reported an instance of dermatitis in a chemist working with penicillin who had a strong reaction to yellow amorphous penicillin but a negative one to the crystalline preparation. In a case reported by Barker [3c] the patient had a positive reaction to a patch test with the commercial penicillin, but a similar solution previously autoclaved failed to elicit a reaction. In the present study, the patients presented eczematoid eruptions localized to the areas of maximum exposure. Removal of the offending agent resulted in prompt recovery, and subsequent exposure in certain instances reproduced the dermatitis. In 3 patients, sensitivity to the active principle of penicillin rather than to the impurities contained in the commercial product was definitely determined.

The development of contact dermatitis to any agent depends on the potency of the allergen, the length of contact and the condition of the skin, rather than to any constitutional or preformed systemic condition.[8] The absence of personal or familial histories of allergy in the present series and negative cutaneous reactions to the Penicillium and Alternaria molds indicate that little connection exists between contact dermatitis to penicillin and clinical allergy to mold. That penicillin contains little if any of the antigen residing in the Penicillium fungus has already been determined.[9]

The patients in this study as well as the majority of those described in the literature have been persons engaged in the manufacture or in the handling of penicillin, rather than patients under treatment with

8. Feinberg, S. M.: Allergy in Practice, Chicago, The Year Book Publishers, Inc., 1944.

9. Feinberg, S. M.: Penicillin Allergy: On the Probability of Allergic Reactions in Fungus Sensitive Individuals; Preliminary Experiments, J. Allergy **15**:271-273 (July) 1944.

the drug. This is readily understood when it is recalled that until recently penicillin was employed chiefly by the parenteral route. No prolonged and repeated contact with the skin or mucous membrane had occurred in the vast majority of patients treated. In our present series we noted that a relatively long period of contact with the allergen (nine to eighteen months) was necessary before sensitization became manifest. It is also conceivable that the skins of persons handling chemicals possess a lower tolerance to allergenic agents than the skin of the average person.

It is not yet entirely clear how potent an allergen penicillin is. McCloskey and Smith [10] were able to produce anaphylactic sensitization to commercial penicillin in guinea pigs. Rostenberg [5] found that repeated injections of penicillin caused an Arthus type of response in the majority of human subjects. In a study of 27 patients receiving prolonged and intensive parenteral treatment, Grolnick and Loewe [11] failed to find any in whom there developed sensitivity to penicillin or to the notatum mold. That penicillin may not be an exceedingly strong allergen is also suggested by the relatively few cases of allergy already encountered in clinical practice and, in the case of dermatitis, by the long period of contact necessary before sensitivity ensues. It is likely, however, that in the employment of penicillin in local therapy there will arise many instances in which such prolonged and repeated contact will be desirable or necessary. In such cases the physician must bear in mind the fact that penicillin is capable of producing an allergic dermatitis of the contact type.

SUMMARY

Contact dermatitis was encountered in 5 persons handling penicillin. A study was carried out in 4 of the cases to determine whether the source of the sensitizing agent was penicillin or the impurities contained in the commercial preparation.

In 3 cases a sensitivity to the active principle of penicillin was definitely determined. No relationship between contact dermatitis due to penicillin and clinical allergy to molds was observed.

Prolonged and repeated contact with penicillin was noted before dermatitis ensued. It is pointed out that similar conditions favorable to the development of contact dermatitis will occur in many patients receiving topical penicillin therapy.

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10. McCloskey, W. T., and Smith, M. I.: Experiments on the Sensitizing Properties of Penicillin, Proc. Soc. Exper. Biol. & Med. **57**:270-275 (Nov.) 1944.

11. Grolnick, M., and Loewe, L.: Immunologic Studies in Patients with Subacute Bacterial Endocarditis Treated by Combined Penicillin-Heparin Method: I. Sensitivity to Penicillin, J. Lab. & Clin. Med. **30**:559-563 (July) 1945.

OBSERVATIONS ON THE CAUSE AND TRANSMISSION OF GRANULOMA INGUINALE

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IN 1937 studies on 8 cases of granuloma inguinale were reported by one of us.[1] In that report it was suggested that a spirochete and a short stout coccobacillary rod might be etiologically related to the disease. It was also suggested in the same report that the disease might be transmitted by means of the pubic louse, Phthirus pubis (Linn.).

It was not until 1943 that studies were resumed along these lines. In the present series all the patients were Negroes, and, with but 1 exception (case 9), all were admitted to Gallinger Municipal Hospital for diagnosis and treatment.

Three pertinent observations appear to have been demonstrated or suggested by this report.

The first observation is that in 10 of the 11 cases (91 per cent) in which the pathognomonic leishmania bodies were found in biopsy material a history of infestation with P. pubis preceding the appearance of the initial lesion was obtained (table). In 3 cases observed by one of us (D. B.) in 1943, in Trinidad, British West Indies, a similar history was obtained. We do not wish to stress the observation that in the 4 cases of this series in which no leishmania bodies could be found the patients gave no history of pubic pediculosis. However, we do wish to emphasize the fact that pubic pediculosis is not rare among Negroes, a fact contrary to common opinion. In this connection it is interesting to note that in 6 of the 11 cases (54 per cent) in which leishmania bodies could be found the initial lesion was extragenital, having appeared in areas frequently infested by P. pubis (pubic and perianal).

A table which accompanied this article has been lost. If it is found, it will be incorporated in the authors' reprints.

From the Department of Bacteriology and Preventive Medicine, Georgetown University School of Medicine (Dr. Butts), and the Rapid Treatment Center, Gallinger Municipal Hospital (Dr. Olansky).

1. Butts, D. C. A.: Am. J. Syph., Gonor. & Ven. Dis. **21**: 544-553, 1937.

The second interesting observation is that in no case in which the patient was married was there a history of the wife's being affected, although several of the patients had suffered from the disease for a period of years (table). The same observation was previously reported by one of us.[1]

The last and most significant observation is one which we feel supports the work recently reported by Anderson, DeMonbreun and Goodpasture [2] and which was suggested by one of us (D. B.) before

Fig. 1 (case 9).—A 19 year old single Negro woman had had the disease for about seven weeks. Serologic reaction was negative for syphilis. Frei and Ducrey tests were negative. Vaginal smears were negative for gonococci. The biopsy material was removed from the ulcerated area underlying the left labium majus (showing pronounced elephantiasis). Observations recorded in figures 2, 3, 4 and 5 were obtained from this case.

the Atlantic Dermatological Conference in February 1944. Rather late in the study of this series of cases (case 9) an attempt to culture

2. Anderson, K.; DeMonbreun, W. A., and Goodpasture, E. W.: J. Exper. Med. **81**:25-39, 1945.

the etiologic agent of granuloma inguinale was undertaken. The disease in this case was at an early stage, the biopsy specimen showing numerous leishmania bodies and typical coccobacillary forms of microorganisms but being free of any spiral forms. Serologic tests for syphilis elicited negative reactions. For these reasons it seemed an excellent case for such a study (fig. 1).

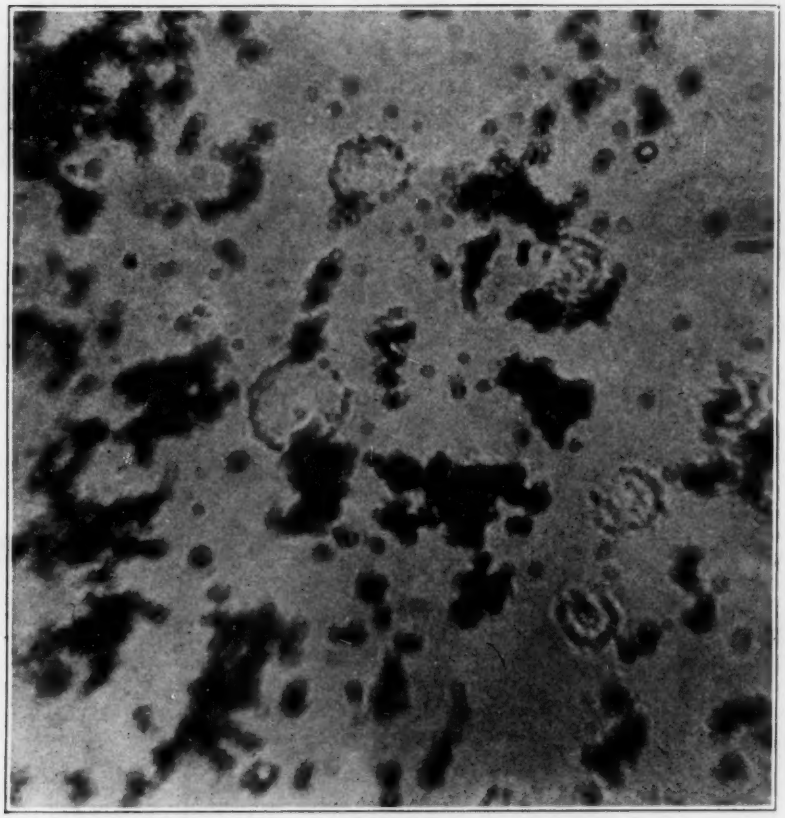

Fig. 2 (case 9).—Gram stain slide from a culture (anaerobic) after four days, growth on ascitic agar. Note rings and clusters of bacteria-like bodies scattered throughout the staphylococci.

Tubes of ascitic agar were inoculated with the tissue immediately on removal from the lesion. These were incubated at 37 C. under aerobic and anaerobic conditions. For anaerobic cultivation, the modified Rosenthal chromium–sulfuric acid method, as suggested by Mueller and Miller,[3] was employed. After four days of anaerobic incubation, there appeared small translucent colonies near the water of syneresis in the tubes.

3. Mueller, J. H., and Miller, P. A.: J. Bact. **41**:301-303, 1941.

Fig. 3 (case 9).—Smear made from biopsy material stained by a modified Machiavello technic. All coccobacillary forms of micro-organisms (deep-staining bodies) were stained red, and all other material throughout the smear was stained blue (× 970).

Fig. 4 (case 9).—Same biopsy material as shown in figure 3. Note clusters of capsulated micro-organisms which were differentially stained red by the modified Machiavello technic (× 970).

Smears made from these colonies and stained by the Gram method showed, in addition to staphylococci, rings and clusters of almost transparent bacillary forms of micro-organisms which, when examined under oblique illumination, appeared to be gram-negative, in striking contrast to the staphylococci (fig. 2).

A subsequent biopsy was made in this case two months later, which afforded interesting data. Smears were made of the tissue and stained with Giemsa stain and also by a slightly modified Machiavello staining technic. The latter method showed small stout coccobacillary micro-organisms occurring singly or in small clusters which retained

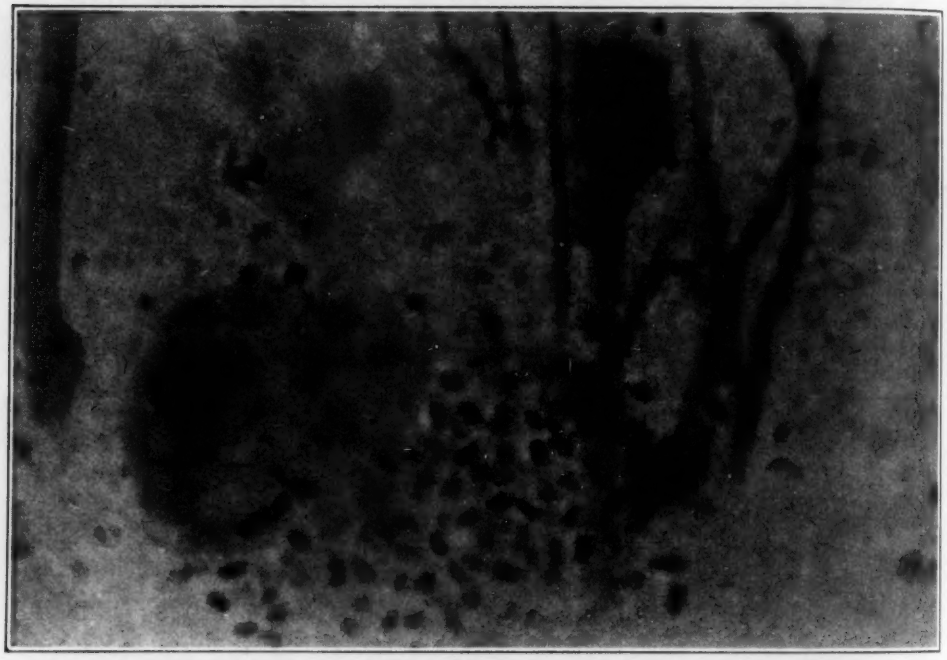

Fig. 5 (case 9).—Same biopsy material as shown in figures 3 and 4, showing a pathognomonic leishmania body stained by the modified Machiavello technic. The deep-staining forms were stained red; the paler forms and the cell nucleus were stained blue (× 970).

the red color of the basic fuchsin. All other micro-organisms and organized structures observed were stained blue (fig. 3). Occasionally some of these would appear as clusters of capsulated organisms of the same general size and shape and displaying the same staining characteristics (fig. 4).

In other fields we observed such clusters of capsulated organisms which were apparently undergoing phagocytosis by large mononucleated cells (macrophages). Finally, these red-staining capsulated micro-

organisms, intermingled with morphologically similar organisms which did not retain the basic fuchsin, could be seen within the cytoplasm of a mononuclear cell (stained blue) and gave the typical picture of a pathognomonic leishmania body (fig. 5). The organisms not retaining the basic fuchsin stain may be nonviable forms.

Similar microscopic observations were likewise obtained in cases 10 (fig. 6) and 11.

It seems possible that the capsulated forms represent the micro-organisms covered with a layer of adsorbed serum, prior to phagocytosis.

Fig. 6 (case 10).—A 25 year old Negro man, married had had the disease for about six months. Serologic tests for syphilis elicited negative reactions. Frei and Ducrey tests elicited negative reactions. Biopsy material removed from the penis when stained by the modified Machiavello technic showed conditions similar to those shown in figures 3, 4 and 5.

In all cases in which there was failure to show any leishmania bodies there was also failure to show any rod forms which were morphologically similar or which retained the basic fuchsin stain when stained by the Machiavello method (cases 9, 10, 11, 14 and 15, table 1).

The modifications in the Machiavello method, as employed in the staining of rickettsias, were in time only. The times used in our studies were as follows: basic fuchsin, two and one-half minutes, citric acid five seconds and methylene blue one minute.

SUMMARY

Considerable evidence has been obtained which suggests that granuloma inguinale may be transmitted during coitus by means of infected pubic lice. It is not, however, suggested that this is the only means of transmission of the disease.

Our observations are in complete agreement with those of Anderson, DeMonbreun and Goodpasture that the etiologic agent of granuloma inguinale is a bacillus. We believe that the name Donovania granulomatis, as suggested by these investigators, would be a most appropriate one for this micro-organism.

Dr. Walter O. Teichmann, chief of the dermatologic clinic at Gallinger Municipal Hospital and associate professor of dermatology and syphilology at Georgetown University School of Medicine, referred several cases to us for study. Dr. Arnold H. Gould, fellow in dermatology and syphilology, Georgetown University School of Medicine and Hospital, referred case 9 to us. Major Charles R. Rein, chief of the division of serology of the Army Medical Center, made the serologic studies on several of these cases, the results of which studies appear in table. The personnel of the photographic laboratory of the Army and Navy Medical Centers contributed all photographic work appearing in this report.

RHINOSCLEROMA

Observations Based on a Study of Two Hundred Cases

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RHINOSCLEROMA (scrofulous lupus of the nostrils, nasal scleroma) is a chronic disease of relatively benign evolution, whose contagiousness is doubtful; it is nonhereditary. Its anatomic characteristic is a tumor formation of varying volume, of waxy or reddish appearance and with a decided tendency to ulcerate and spread. It is invariably located in the rhinopharyngeal region.

HISTORY

In the Museum of the History of Medicine, of Cracow, Poland,[1] there are wax models of this disease made in the year 1840, which were exhibited by Bierkowsky as cutaneous cancers. Hebra [2] (1870) was the first to make a clinical description of this curious disease, naming it rhinoscleroma (hard nose). At that time it was mistaken for syphilis and sarcoma. Geber [3] in 1872 and Mikulicz [4] in 1876 histologically demonstrated its sclerotic tissue. In 1882 Frisch [5] discovered an encapsulated bacillus which now bears his name and which he considered to be the main cause of the disease.

INCIDENCE

Rhinoscleroma is widespread (more so than is generally supposed) in Europe, in Russia, Poland, Switzerland, Austria, Italy, Spain, Sweden and other countries. In North America there are a few cases to be found among immigrating races but rarely among natives. In South America, as well as in the West Indies, there have been several

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1. Watrin, J., in Darier and others: Novelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 4.

2. von Hebra, F.: Rhinosclerom, Wien. med. Presse **11**:445, 1870.

3. Geber, E.: Ueber das Wesen des Rhinosclerom; eine klinisch-histologische Studie, Arch. f. Dermat. u. Syph. **4**:491, 1872.

4. Mikulicz, J.: Ueber das Rhinosclerom, Arch. f. klin. Chir. **20**:485, 1876-1877.

5. von Frisch, A.: Zur Aetiologie des Rhinoskleroms, Wien. med. Wchnschr. **32**:969, 1882.

cases reported; however, it is in Central America (El Salvador and Guatemala) that cases of this disease are most frequently found.

ETIOLOGY

Rhinoscleroma affects both sexes, but is predominant among women. In my experience with 200 patients, 120 were women. All of them were peasants, of poor hygienic habits, with the exception of 2 who proved to be city residents of doubtful hygienic habits.

The true agent causing this disease is not definitely known. It was attributed by Frisch to a bacillus of Friedländer type, which is to be found in regular quantities in some cases of rhinoscleroma. Notwithstanding, I have found this bacillus in patients attacked with rhinitis, without scleroma. It is probable that Klebsiella ozaenae and Friedländer's bacillus (Klebsiella pneumoniae) are present in large numbers in the pathologic conditions of these mucous membranes.

For many years I have tried to reproduce rhinoscleroma in laboratory animals, as well as in human beings, through inoculation and grafting, without success. Now my research work is focused on the theory that rhinoscleroma is caused by a filtrable virus.

The contagiousness of rhinoscleroma has been widely discussed; there are on record several cases which would appear to be a solution to the problem, such as those described by Lasagna, of 15 Italians who had rhinoscleroma (?), all of them members of the same family and dwelling in the same home. Among my cases, numbering 200, I have found only the case of 2 brothers who contracted rhinoscleroma, the one four months after the other.

BACTERIOLOGY

Frisch found in the nasal secretion from a person having rhinoscleroma an encapsulated diplobacillus, from 2 to 3 microns in length and from 0.5 to 1 micron in width, which when strained with Gram's stain appears light red and surrounded by a clear halo, the capsule. These characteristics do not belong exclusively to the Frisch bacillus (Klebsiella rhinoscleromatis) but belong to other encapsulated bacilli as well, such as the K. ozaenae and K. pneumoniae, which are found in the nostrils and which are responsible for adding to the confusion in establishing whether or not the Frisch bacillus is the real cause of this disease. Personally, I am of the opinion that the histologic and clinical observations are the only means of making the correct diagnosis of rhinoscleroma.

Cultures are made in gelose, and for this purpose an incision is made in one of the nodules and the blood flowing from the cut is used. The culture tube should be kept at a temperature of 37. After twenty-four hours, small colonies begin to appear, taking the shape of a button;

some are light yellow, and others are stearine white. Besides being made in gelose, cultures can be made in milk, on potato or in ordinary broth.

PATHOLOGY

The histopathologic structure of rhinoscleroma is characterized by three elements:

1. Plasmocytes infiltrate massively, occupying a large portion of the dermis and separating it from the epidermis by means of a thin zone of lymphatic cells.

2. Mikulicz cells, rounded elements, 50 microns in diameter, are found among the infiltrated plasmocytes. They appear pale, and almost transparent, with somewhat fading contours. In some of these cells the Frisch bacilli are to be found. In these cells is also noted a rounded curdling, which becomes intensely colored, is ordinarily located in the marginal zones and is classified as the nucleus. These cells are considered degenerated plasmocytes.

3. Strang elements, Russell bodies, also are found among the plasmocytic infiltration. They are from 20 to 40 microns in diameter and have been classified as degenerated hyaline bodies by Unna and Pellizari. These bodies are spherical and become intensely dark colored.

The histopathologic features of this disease vary in accordance with its different stages. Thus, for instance, in its secondary stage the presence of Russell bodies in regular quantities is also observed, in addition to the plasmocytic infiltration, while Mikulicz cells are very rare. The third stage is richer in details; at the beginning of this stage the Mikulicz cells start to be more abundant. The numerous dilated vessels are observed to have sclerosed walls; this sclerosis is sometimes so advanced that it completely obliterates the vessel. In more advanced cases of the third stage, a sclerotic tissue is noted as invading the entire field and segregating the plasmocytes in groups in which the Mikulicz cells are abundant; Russell bodies are rarely found here.

SYMPTOMATOLOGY

Rhinoscleroma is a chronic disease appearing in both sexes, predominantly among women. It makes its first appearance in persons between 20 and 40 years of age, being very rare among persons under 15 and over 50 years of age. The course of this disease, according to my statistical records, fluctuates between eight and twenty years.

The disease localizes itself in the rhinopharyngeal region, transforming the countenance of these patients to the extent of resembling a rhinoceros or a hippopotamus; it is never accompanied with fever. The patient's general condition is not affected, and the majority of persons

attacked are of the strong build type. It is hard to estimate accurately its period of incubation, and the development of its symptoms is gradual.

In view of the foregoing facts and for a better study of rhinoscleroma, I shall divide it into three stages:

First Stage.—Rhinitis Period: In the majority of cases, the disease makes its appearance with all the symptoms of a coryza with fronto-ethmoidal cephalalgia, followed by rather difficult respiration; there is scant nasal secretion, more or less fetid. The patient complains of dryness of the throat. Rhinoscopic examination reveals a red mucous membrane already hypertrophic; that of the septum is particularly involved, as it is here that the infiltration first appears. While going through this period patients seldom call for medical advice and inexplicably will keep quiet about these troubles for months in succession. Most of the patients call on the physician for consultation only after the second period begins, that is, when mechanical phenomena appear (difficult respiration and others).

Second Stage.—Infiltrating Period: The symptoms of coryza begin to disappear, leaving characteristic marks in those places where the infiltration localizes itself. In order of frequency these are: nasal septum, lower part of the nostrils and larynx. The septum thickens to the extent of making respiration difficult, this obstruction being incomplete if it affects one side and total if it affects both sides. At the lower part of the nostrils there appear waxy or reddish infiltrations (fig. *A*). Finally, laryngeal infiltration takes place, causing changes to occur in the modulations and intonations of the voice. In the majority of cases of the second period complete anesthesia of the soft palate is discovered, a sign that is diagnostic.

Third Stage.—Nodular Period: This is the period of exaggerated or total spreading of the aforementioned second period. In this manner, then, rhinoscleroma localizes in the septum and progresses upward, exaggerating the appearance of the nose and sometimes causing monstrous deformities, as shown in the figure (*B*). When the invasion progresses upward difficulty in respiration is not total, as the patient can inhale through the nose and the mouth. When the invasion progresses toward the bottom (floor) of the nostrils, it shows a decided trend to obstruct them completely; then the patient's voice takes on a deep twang; there are anosmia and epistaxis; the roof of the mouth becomes pale, and the palatal arch disappears, showing a tumor formation. The localization of the disease at the lower part of the nostrils shows a peculiar tendency to progress anteriorly, invading the lobe and wings of the nose, the upper lip and the alveolus. When the condition has reached this stage and the invasion is well advanced, the patient presents a repulsive appearance, as seen in the figures (*C* and *D*), resembling that of a hippopotamus. In such cases, staphylococcic

secondary infections are frequent; the lips become enlarged because of rhinoscleromatic infiltration, resembling the labia majora in cases of common elephantiasis due to venereal lymphopathies.

Rhinoscleroma: *A*, waxy nodules below nares. *B*, advanced stage, showing rhinoceros-like projections. *C* and *D*, advanced stages, showing hippopotamus-like projections.

When laryngeal infiltration occurs, the patient's voice becomes bitonal, and as the infiltration progresses the voice disappears completely and respiration grows more painfully difficult to the extent of making

tracheotomy necessary. The process of scleromatous infiltration covers the larynx and pharynx, until some intercurrent disease causes death.

As stated before, these three periods take many years to reach full development. In some cases of localization in the nostrils, the growths ulcerate, yielding a yellow fetid secretion. When the disease is well advanced, these conditions are followed by destruction of bone which affects the septum and the superior and inferior conchas of the nose, as well as the maxillary and ethmoid sinuses.

In cases of rhinoscleroma, the hemogram presents no abnormalities.

There are cases on record, mainly those of the disease localized in the septum, in which there was a spontaneous regression, leaving behind an atrophy in the nose. I have observed such regression to occur, however, only during the first period of infiltration.

DIAGNOSIS

The diagnosis is based on the clinical appearance and on the histopathologic structure which are characteristics of this disease, thus differing from all other diseases of the skin (plasmocytic infiltration and Mikulicz cells). However, from the clinical standpoint, syphilis, ozena, sarcoma, mutilating rhinopharyngitis and snuffling goundou should be considered. In some cases, I have found false positive Wassermann reactions; there are also cases of combined syphilis and rhinoscleroma in which the preliminary treatment helps to establish the diagnosis. The differential diagnosis from sarcoma is made through coloration. The ligneous hardness, the painlessness, and slowness of evolution and the absence of ganglionic infarcts are diagnostic of rhinoscleroma. And, to complete the work, a complement fixation test may be resorted to, in view of the presence of Frisch's bacillus. The Forges-Elbert agglutination test as well as an intradermal test with toxin of Frisch's bacillus, may be tried.

PROGNOSIS

The disease is of long duration and curable, provided the patient calls on the physician at an early stage and provided the latter makes the diagnosis at the beginning of the period. Mortality varies in accordance with the localization and extension of the lesion. Thus, for instance, for patients with laryngeal localization with extension to the trachea asphyxia by obstruction is the constant threat and prompt intervention is required (tracheotomy) to save the patient's life. There may be recurrences, and when the disease is of long duration the patients may end with pulmonary tuberculosis, or the lesions may be transformed into malignant neoplasmas. In some cases, the lesions remain stationary, to become reactivated by some traumatism or infection.

PROPHYLAXIS

Rhinoscleroma is a disease contracted through poor personal hygiene; it is never found among people of absolutely clean habits. Its contagiousness is doubtful. Among my cases and through my years of study of this disease, I have not yet encountered a single case that I could have unhesitatingly classified as contagious; I did, however, prove beyond any doubt that all my patients observed very poor hygiene both personal and in the home.

TREATMENT

The monstrosity of this disease is responsible for innumerable treatments and procedures in the countries in which it is known to exist; it would take too long to enumerate them. All have no therapeutic value against this disease. Thus it happens that these patients have been treated with all sorts of mercurials, caustics (zinc chloride, lactic acid, pyrogallol, iodine, silver nitrate, salicylic acid), arsenicals, bismuth preparations, chaulmoogra oil, antimony and potassium tartrate, vaccines (autovaccines), autohemotherapy, proteinotherapy, interstitial injections of iodine, methylthionine chloride, electrocoagulation, cautery, surgical extirpation, curettage or the so-called pruning system. After the last system has been applied, the infection progresses with greater aggressiveness.

Among my cases, the only treatment giving excellent results, to the extent of permitting this disease to be considered curable, is roentgen irradiation, given in sessions of seven applications with the following technical factors: 200 kilovolts; filtered through 0.5 mm. of copper and 1 mm. of aluminum; focal skin distance, 50 cm.; dose, 200 r per day, during seven consecutive days; total dose, 1,400 r and fields, one—anteroposterior over the nose. The reaction is light erythema, followed by hyperpigmentation which disappears after three months.

Five applications should be given per year during the first and second stages, for two years. In the third stage, the prognosis for complete healing is reserved, but I have succeeded in keeping my patients in good condition, so that they could work and keep on living their routine, normal lives.

Surprising results have also been obtained through intramuscular injections of azosulfamide (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene 3′, 6′-disulfonate).

In conclusion, at the present time the only effective therapeutic agents to combat rhinoscleroma are roentgen rays and azosulfamide.

MAMMALIAN PIGMENTATION

The Problem of the Pigmentary Mechanism Studied by Means of the Respiration of Tissues

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THE MECHANISM of pigmentation in the lower animals has been fairly well established. Some of the precursors of the melanin compounds have been isolated, and the enzyme tyrosinase has frequently been identified in extracts from tissues of these lower animals. In them, it is thought that the formation of melanin proceeds from the naturally occurring amino acid tyrosine and involves enzymatic catalysis, with tyrosinase as the active enzyme. Raper and Evans [1] gave a logical series of enzymatic and chemical reactions for the pigmentation mechanism.

However, tyrosinase has rarely been isolated from pigmented tissues of mammals, with the result that considerable confusion exists concerning the enzyme active in mammalian pigmentation. Bloch's [2] extensive work on the pigmentary mechanism in the human being led many to favor his theory of the existence of a special oxidase (dopase)-producing melanin in human beings by action on a prepigment *l*-3, 4-dihydroxyphenylalanine (dopa). On the other hand, Meirowsky [3] came to the conclusion that no dopa oxidase exists, preferring to accept an unspecific polyphenoloxidase or a chemically characterized catalyst as a more likely actor in the production of melanin. Schaaf,[4] too, suggested a similar

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From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, and the Institutum Divi Thomae, Cincinnati.

1. Raper, H. S.: Some Problems on Tyrosine Metabolism, J. Chem. Soc., 1938, pp. 125-130. Raper, H. S., and Evans, W. C.: A Comparative Study of the Production of *l*-3:4-Dihydroxyphenylalanine from Tyrosine by Tyrosinase from Various Sources, Biochem. J. **31**:2155-2170, 1937. Evans, W. C., and Raper, H. S.: The Accumulation of *l*-3:4-Dihydroxyphenylalanine in the Tyrosinase-Tyrosine Reaction, ibid. **31**:2162, 1937.

2. Bloch, B.: The Problem of Pigment Formation, Am. J. M. Sc. **177**:609-618, 1929.

3. Meirowsky, E.: A Critical Review of Pigment Research in the Last Hundred Years, Brit. J. Dermat. **52**:205-217, 1940.

4. Schaaf, F.: Manometrische Vergleichsuntersuchungen mit Presssäften aus weisser und pigmentierter Meerschweinchenhaut (Beitrag zur Blochschen Dopatheorie der Pigmentgenese), Arch.f.Dermat.u.Syph. **176**:646-688, 1938.

mechanism, for he found that extracts of skin oxidize not only dopa but also catechol, hydroquinone, *d*-3,4-dihydroxyphenylalanine and at times even *p*-cresol.

Recently, Hogeboom and Adams,[5] using extracts from the Harding-Passey mouse melanoma, a tumor composed of melanin-producing cells, showed that enzymes were present which oxidized dopa and *l*-tyrosine. They obtained two fractions, one of which was active in oxidizing dopa but was unable to oxidize tyrosine, hydroquinone and *p*-cresol, and the other an insoluble fraction which oxidized tyrosine but failed to oxidize phenol, hydroquinone and *p*-cresol.

The present studies include use of the Harding-Passey mouse melanoma. We worked with the tissue itself rather than with extracts. It is hoped that thereby the in vivo essentials of the enzymes or catalysts present in the tissue are preserved. In order to control the interpretation of the results, identical studies with nonpigmented tumors were also made.

PROCEDURE

Tissue slices of the Harding-Passey mouse melanoma were used in the studies of the pigmentary process; comparable studies were made with tissue slices of mouse sarcoma 180 of albino mice, the Bar Harbor adenocarcinoma of dba mice and the ears of guinea pigs. All the animals were killed by a sharp blow over the base of the skull. The tissues were removed immediately and placed in Ringer's solution (0.2 per cent dextrose). The solution was buffered to p_H 6.5, instead of the usual 7.3, in order to prevent auto-oxidation of the dopa solutions used in some of the experiments.

The tissues were carefully freed of all connective tissue and cut into sections approximately 1 cc. in volume, and the sections were placed in the manometer flasks. The respiration was measured at 37.5 C. in air, by the direct method,[6] the constant volume type of Warburg manometer being used. Seven manometers were used in the experimental runs, one for the thermobarometric control and the remaining six for tissue controls and for testing the effects of added solutions.

The solutions to be tested were placed in the side arms of the manometer flasks. After an equilibrium period of fifteen minutes, the oxygen consumption of the tissue was measured during a control period of forty-five to sixty minutes, readings being taken every fifteen to thirty minutes. Then the test solutions were tipped into the flasks from the side arms, and the oxygen consumption was measured for one and a half hours, readings again being taken every fifteen to thirty minutes. The tissues were then carefully removed from the flasks, washed in distilled water and dried to a constant weight at 100 C. From 25 to 35 mg. (dry weight) of tissue was used in each flask. The carbon dioxide produced by the tissues was measured "by rates,"[7] the direct method again being used. The solutions tested were: (1) dopa, 0.05 and 0.1 per cent; (2) potassium cyanide

5. Hogeboom, G. H., and Adams, M. H.: Mammalian Tyrosinase and Dopa Oxidase, J. Biol. Chem. **145**:273-279, 1942.

6. Dixon, M.: Manometric Methods, ed. 2, New York, The Macmillan Co., 1943.

7. "By rates" refers to the manner of recording the amounts of carbon dioxide liberated in a series of successive fifteen minute intervals of time.

and (3) sodium fluoride, each 0.001-molar and 0.01-molar; (4) *p*-cresol, 3 mg. and 5 mg. The values given for these substances refer to the concentrations or the quantities present in the manometer flasks after these solutions were tipped from the side arm.

RESULTS

The results given in table 1 show that with the mouse melanoma dopa invariably stimulates the uptake of oxygen and the liberation of carbon dioxide. This points to an enzymatic rather than to a simple chemical catalytic operation in the oxidation of dopa. The increased production of carbon dioxide suggests further that there is in the tissue

TABLE 1.—*Influence of Dopa on the Respiration of Melanoma Tissue (Harding-Passey Mouse Melanoma)*

Period *	Melanoma, Cu. Mm. per Mg. per Hr.		Melanoma * Dopa 0.1% Cu. Mm. per Mg. per Hr.	
	Q_{O_2}	Q_{CO_2}	Q_{O_2}	Q_{CO_2}
Control	0.545	0.263	0.468	0.366
Experimental	0.426	0.217	0.953	0.508
Per cent change—experimental over control	—22	—17	+104	+42

* The words "control" and "experimental" as referable to the periods of respiration refer to the first and the second halves of the respiration run, during the latter of which dopa was added to some of the melanoma tissue.

TABLE 2.—*Influence on the Uptake of Oxygen of Tissue on Addition of Dopa, Potassium Cyanide (KCN) and Sodium Fluoride (NaF)**

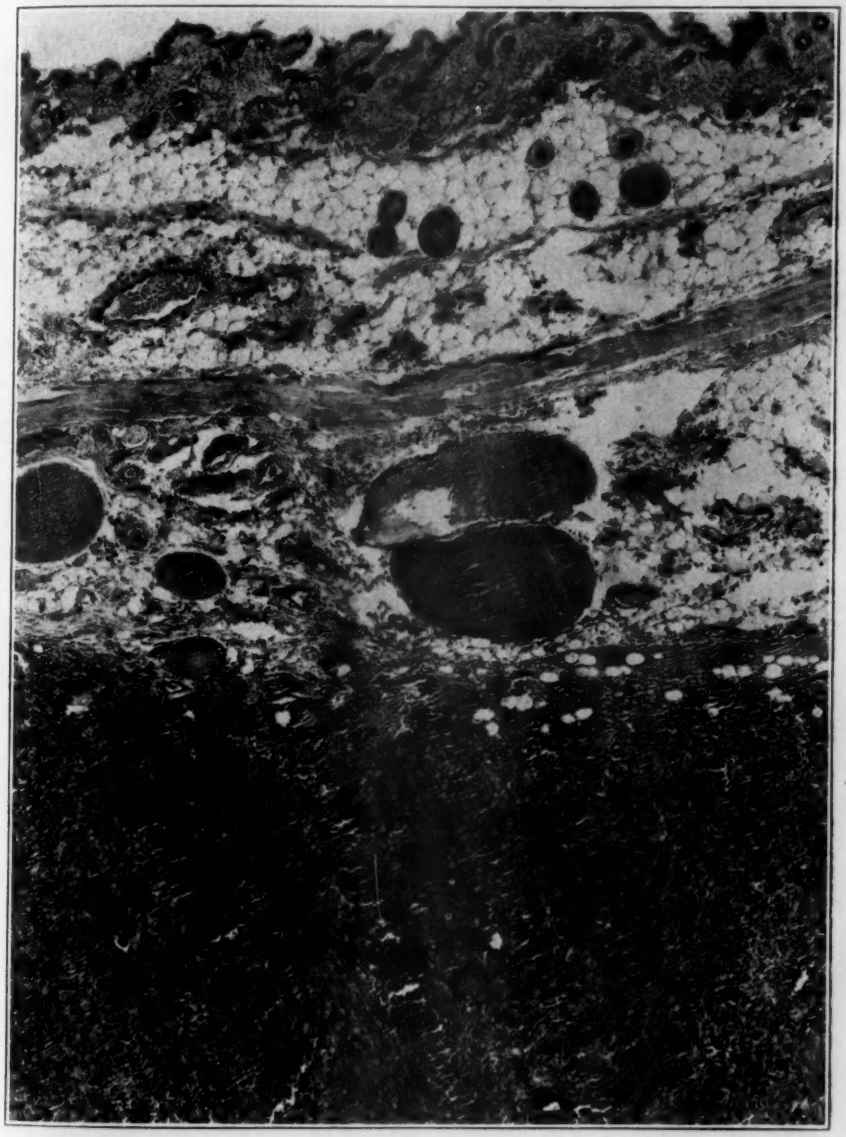
Tissue	Dopa 0.05% Concentration	KCN 0.01-M Concentration	KCN + Dopa 0.01-M + 0.05% Concentration	NaF 0.01-M Concentration	NaF + Dopa 0.01-M + 0.05% Concentration
Mouse melanoma	+63%	—50%	—61%	—51%	+21%
Mouse adenoma	—17%	—28%	—40%	—76%	—81%
Mouse sarcoma 180	—33%	—53%	—44%	—60%	—76%
	(a) 0.05% Conc. (b) 0.1% Conc.	0.001-M Conc.		0.001-M Conc.	
Guinea pig skin (ear)	(a) —15% (b) +11% within experimental error	—54%	—56%	—19%	—26%

* Expressed as percentile stimulation (+) or inhibition (—) of the control tissue respiration.

a substrate akin to dopa and/or that a redox system operates within the mechanism of pigment formation.

As revealed by table 2, dopa causes an inhibition of the oxygen uptake of the nonpigmented tumors, both sarcoma 180 and the adenoma. This strongly suggests that dopa's stimulation of the respiration of the melanoma is connected with the pigmentary process. The addition of potassium cyanide and sodium fluoride causes an inhibition of the uptake of oxygen in all tissues. The same depression tends to prevail after dopa is added to the mixtures containing potassium cyanide and sodium fluoride. However, note should be taken of the fact that when

dopa was added to the mixture containing sodium fluoride the latter failed to suppress completely the stimulation expected from dopa. These observations are further indications of an enzymatic process



Photomicrograph showing the Harding-Passey mouse melanoma. The melanotic growth is so infiltrated by melanin particles as to mask completely in places the cells that produce these particles.

underlying the oxidation of dopa and, under the conditions of the experiments, of the sensitivity of the enzyme to cyanide and fluoride poisoning.

Attention is called to the feeble response of the skin (the ear of a guinea pig) following exposure to dopa. Efforts to study the pigmentary process in healthy skin by the monometric procedure have repeatedly given measurements within the limits of experimental error, and this fact directly accounts for the necessity of resorting for study to the type of tissue (melanoma) reported on in this paper. Normal skin obviously contains too little of the pigmentary materials to reveal meaningful data by procedures now available.

Mouse melanoma *Brei* (pulp) disclosed an almost complete loss of capacity to take up oxygen, but addition of dopa caused a considerable increase in the uptake of oxygen. The further addition of potassium cyanide caused complete inhibition of this stimulation. Here, too, is supportive evidence of an enzymatic process in the oxidation of dopa.

Several experiments with mouse melanoma and added *p*-cresol gave equivocal results, at times a stimulation of respiration and at others a depression. The production of carbon dioxide was regularly depressed. This experiment sought to discover evidence in behalf of tyrosinase as the enzyme concerned in these reactions. It may well be that significant variations in the concentrations of the enzymes in the several melanoma tissues used accounted for the contradictory findings.

SUMMARY

The data presented lead to the following conclusions in respect to the pigmentary process in mammals:

1. The process requires an enzymatic step.
2. Dopa may be the actual prepigment involved.
3. No definite conclusions can be drawn as to the specific character of the enzyme in operation, although the evidence suggests the presence of tyrosinase.

As referable to the character of the enzyme, attention is directed to the fact that these studies were carried out with the solution containing the tissues at a p_H of 6.5, probably nonoptimal for the process under investigation. While this degree of acidity was used to prevent autooxidation of dopa, it may have interfered with attempts to elicit distinguishing characteristics of the enzyme.

DIAGNOSTIC SIGNIFICANCE OF THE CULTURE METHOD IN CUTANEOUS LEISHMANIASIS (ORIENTAL SORE)

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CULTURES of the leishmania parasite were first made by Nicolle,[1] and the customary method is to use on the N. N. N. (Nicolle Novy-McNeal) medium. Culture is, however, as a rule, used for laboratory transmission and therapeutic experiments while only rarely has it been employed as an aid in clinical diagnosis.

In countries where the disease occurs endemically there are always numerous cases which, although clinically they may arouse the suspicion of leishmaniasis, require confirmation by objective methods by which the parasite can be demonstrated. This applies particularly to the ulcerative lesions of long standing and to relapsing leishmaniasis, in which it is generally impossible to demonstrate the parasites in smear preparations. In these recurrences which clinically show a striking resemblance to lupus and to tertiary syphilis and in which it is equally difficult to discover the parasites, it is of greatest importance to be in possession of a method by which it is possible to establish an objective diagnosis. Neither can the histologic picture, which in these types often has a tuberculoid structure, be used to decide the differential diagnosis.

We have, therefore, in a number of cases studied the diagnostic significance of the culture method and are, in the following presentation, giving the results of these studies:

EXPERIMENTAL SETUP

We used Adler's modification of Noguchi's medium[2] consisting of:

	Parts
Agar (2.5 per cent)	1
Locke's solution containing 0.1 per cent of dextrose	8
Fresh rabbit blood	1

From the Dermatological Department of the Hadassah-Rothschild University Hospital, Jerusalem, Palestine, Dr. A. Dostrovsky, Director.

1. Nicolle, C.: Culture du parasite du bouton d'Orient, Compt. rend. Acad. d. sc. **146**:842, 1908.

2. Adler, S., and Theodor, O.: The Identity of Leishmania Tropica Wright, 1903, and Hepetomonas Papatasii Adler, 1925, Ann. Trop. Med. **20**:355-364 (Dec. 17) 1926.

(In some cases the specimens were taken, and cultures set up in the hospital; the cultures, however, were transferred for further bacteriologic study to the Bacteriologic Institute [Director: Dr. Gurevitch] while in others the patients were sent to the Parasitologic Institute [Director: Professor Adler] and the whole process of culturing carried out there.) Specimens were taken by making small cuts into the lesion, usually at the edge—in no case in the suppurating or ulcerating center. A small glass capillary tube to which a rubber ball was attached was then placed into one of these cuts. Since the prospects of obtaining positive cultures from blood alone are negligible, it was tried, by slight to-and-fro motion with simultaneous aspiration, to detach minute shreds of tissue. The material thus obtained was then transferred to the culture medium and kept at a temperature of 22 C. Complete sterility is important, since the culture medium is susceptible to contamination. Several tubes should be inoculated at the same time. If the parasites are numerous, they grow on the cultures within the course of a week. In the cases referred to, in which the smears contained no or only isolated parasites, so that their identification was impossible, a definitely positive culture occasionally required as long as three weeks.

Subjects.—The total number of cases in which cultures were made was 61, in several of which the procedure had to be repeated after a negative result had been obtained on the first occasion.

The first group, comprising 26 cases, was of the early stage of leishmaniasis, while a further 30 were of recurrent leishmaniasis, and in 5 the material was obtained from scars after healing had already taken place.

RESULTS

In 10 cases in which smears yielded positive results, cultures were also invariably positive. In two of the positive smears, the cultures showed secondary infection; hence the results were negative. In 8 cases which were in the last few months before spontaneous healing could be expected to take place and in which microscopically no parasites

TABLE 1.—*Comparison of Results in Smear Preparations and in Cultures in 26 Cases of the Early Stage of Cutaneous Leishmaniasis*

	Number of Cases
Positive in smears and cultures	10
Positive in smears, negative in cultures	2
Negative in smears, positive in cultures	8
Negative in smears, negative in cultures	6
Total	26

were found, cultures were still positive. In the remaining 6 cases in which cultures as well as smears were negative, three cultures showed repeated contamination; one was of the annular type of leishmaniasis with only a positive cutaneous reaction and two remained negative although there was no contamination. Contamination usually occurred in material taken from suppurating boils, so that clean material could not be obtained even from the edge of the lesion. These early types with

their frequent secondary infection offer much technical difficulty, while, on the other hand, this is of no consequence, since in such cases the differential diagnosis is more rarely fraught with difficulty.

Conditions are different in cases in which long-standing lesions or recurrences in long-standing scars are concerned.

In connection with the question of recurrence *in loco,* we studied 5 cases of cutaneous leishmaniasis which, from a clinical viewpoint, could be declared as cured. Cultures as well as smears were negative

TABLE 2.—*Comparison of Results in Smears and Cultures in Thirty Cases of the Late Stage of Cutaneous Leishmaniasis (Leishmaniasis Recidiva)*

	Number of Cases
Positive in smears, positive in cultures	2
Positive in smears, negative in cultures	0
Negative in smears, positive in cultures	18
Negative in smears, negative in cultures	10
Total	30

in all of them, while the intracutaneous leishmania vaccine elicited a positive reaction.

In 1 of the cases cultures were exclusively set up for the purpose of demonstrating that healing had actually taken place, so that there remained 29 cases with an active process. Cultures were positive in 20 of them and negative in 9. In the smears, parasites were found in 2 instances only, and it must be pointed out that no more than one or two parasites could be detected and this only after a search of several hours. Only an experienced examiner was able to identify them as leishmania parasites at all.

In 60 per cent of this group, therefore, definite evidence of the leishmania nature of the lesion was supplied by the culture method alone.

This is illustrated by the following cases:

REPORT OF CASES

CASE 1.—The patient was a boy of 11 years. He was born in Baghdad. When he was 2 years old, he had had two lesions on the right forearm, now marked by two scars. We were probably dealing with healed lesions of leishmaniasis. Since his seventh year, he had had a lesion on his nose (fig. 1.)

Examination.—There was a lesion occupying the entire distal portion of the right half of the nose, here and there spreading to the left side consisting of flat infiltrations dissolving at the outer border into isolated small papules. To the right of the tip of the nose there was a slightly elevated area of granulation. The infiltrations had a reddish brown tinge. In one place scar tissue was noted. Pressure by a glass spatula revealed a multitude of tiny papules of a yellowish tinge in the depth.

A Mantoux test (old tuberculin in a dilution of 1:50,000) elicited a positive reaction. A test with Leishmania vaccine elicited a positive reaction. Microscopic

examination revealed no bacteria. Growth of Leishmania parasites appeared on cultures after three weeks.

Comment.—The localization and the aspect of the lesion confronted us with a differential diagnosis between cutaneous leishmaniasis and lupus vulgaris. No parasites could be demonstrated, but the intracutaneous test for leishmaniasis

Fig. 1.—Lupus-like leishmaniasis. Culture was positive for Leishmania parasites.

Fig. 2.—Serpiginous recurrent leishmaniasis. Microscope revealed no parasites but culture was positive.

elicited a positive reaction. Since, however, the patient had already had a leishmania lesion on his forearm when he was 2 years old, the result of the test was not decisive. The tuberculin test elicited an equally positive reaction. Thus only the identification of the parasites in the cultures provided the decisive evidence.

CASE 2.—The patient was a 12 year old girl who was born in Baghdad and had been in Palestine for seven years. She presented lesions on both cheeks, which had been present since the age of 1 year.

Examination.—The patient (fig. 2) presented on the anterior portion of the right cheeks two coalescing lesions consisting of a reddish brown infiltration with serpiginous spread to the periphery, while in the center spontaneous healing had already set in. Below this lesion there was an oval, sharply outlined scar with a small infiltration at one point of the edge, and above there was a second, smaller, scar with beginning infiltration. To the right of the mouth, there was a small punched scar. The left cheek offered essentially the same aspect, though of lesser intensity.

A Mantoux test (old tuberculin in a dilution of 1 : 50,000) elicited a negative reaction. An intracutaneous test with a leishmania vaccine elicited a positive

Fig. 3.—Recurrent leishmaniasis with no parasites and rare localization on the lips. Cultures were positive for the parasites.

reaction. There were no leishmania parasites in smears (three examinations). Leishmania bacteria grew on culture.

Histologic Examination (Pathological Institute, Director: Professor Franco).—Granulation tissue of a tuberculoid type was found with typically tuberculous structure without caseation. Examination revealed no mycobacterium tuberculosis and leishmania parasites.

Comment.—The patient presented lesions which, clinically, bore much resemblance to the serpiginous type of lupus. The scars which were sharply punched with their recurrent papules were, here in this country, suggestive of cutaneous leishmaniasis. The objective evidence was supplied only by the cultures, since no parasites could be demonstrated either in smears or by histologic examination.

Case 3.—The patient was a girl of 15, born in Baghdad. For seven years she had had lesions which grew slowly. She had received injections (antimony?) and roentgen ray therapy but without effect.

Examination.—There were seven lesions on the face (fig. 3): on the forehead, the nose, the upper and lower lips and the outer angle of the right eye as well as two on the left cheek. All the lesions showed distinct reddish brown infiltrations which, on the nose, showed a tendency to ulceration with serpiginous spread on the cheek. There were two similar lesions on the arm and two on the leg.

A Mantoux test (old tuberculin in a dilution of 1: 50,000) elicited a positive reaction. An intracutaneous test with leishmania vaccine elicited a positive reaction. Several examinations revealed no parasites. Culture was positive for Leishmania after three weeks.

Fig. 4.—Recurrent leishmaniasis appearing in gumma fashion, with parasites present on culture.

Histologic Examination (Professor Franco).—"The epidermis of the lesion on the arm is hypertrophied. The cutis contains several circular lesions, lying very close together and showing a granulomatous structure similar to that of chronic tuberculosis without caseation. Langhans' giant cells are present in abundance. No Leishmania parasites can be demonstrated."

Comment.—The patient presented a total of eleven lesions on various parts of her body. Although the clinical aspect was typical of recurrent leishmaniasis, the histologic picture and the reaction to the tuberculin test were in an equal measure suggestive of tuberculosis, and it was only by the positive results of cultures that the bacteriologic evidence could be provided.

Case 4.—The patient was an Arabian boy, aged 17, from Ramallah, a small town in the neighborhood of Jerusalem. Three years earlier a small papule had developed on his right cheek, which grew and ulcerated rapidly. In the course of one year, however, healing was complete. A short time later new lesions appeared on the right as well as on the left cheek, which spread systematically,

leaving pigmented scarring. When we saw the patient, both cheeks, particularly the left, were involved (fig. 4). There was active infiltration of the edges in the neighborhood of the eyes and nose, while on the opposite side, toward the mandible, the lesions had already disappeared leaving scars. The spread was similar to that of tertiary syphilis. The entire upper lip was swollen to twice its original size and occupied by a deep infiltration, here and there spreading to the red portion. A similar lesion existed on the left auricle.

An intracutaneous test with Leishmania vaccine elicited a positive reaction. There were no Leishmania parasites in smears. Cultures were positive for Leishmania parasites. Wassermann and Kahn reactions were negative.

Histologic examination of specimens from the right cheek and ear revealed tuberculoid granulation tissue.

Comment.—The patient presented lesions on the cheek and on one ear, spreading in a typical serpiginous way and forming reddish brown infiltrations in gumma fashion. No parasites could be demonstrated in the smears, and in the histologic examination no distinction from tuberculosis or gumma was possible. The reaction of the intracutaneous test as well as the cultures were positive for leishmaniasis.

COMMENT

In 61 cases of cutaneous leishmaniasis (Oriental sore) cultures for diagnostic purposes were set up. Although in the majority of the cases it could be assumed, in view of the clinical aspect and the results of diagnostic methods (histology, reaction to Leishmania vaccine, history, etc.)—especially here in this country—that we were dealing with cutaneous leishmaniasis, the final evidence was still lacking. Among 26 cases of early disease the parasites could be demonstrated exclusively by culturing in 8 instances, and the same was true in 18 out of 30 cases of recurrent leishmaniasis. Five of the patients presented scars after healing had already taken place.

Although the data are not numerous, they clearly underline the diagnostic significance of the culture method.

The difficulty of demonstrating the parasites in smears in the clinically deviating types of cutaneous leishmaniasis has repeatedly been stressed. Dostrovsky [3] reported positive evidence of parasites in only 1 out of a group of 6 cases of recurrent leishmaniasis. Maschkileisson, Neradov and Rapoport [4] were unable to detect parasites in any of their 9 cases of lupoid leishmaniasis. Berlin [5] reported positive findings in 3 among 13 cases. Smith [6] pointed out that in late recurrences

3. Dostrovsky, A.: Relapses in Cutaneous Leishmaniasis, Ann. Trop. Med. **30**:267-274 (Oct. 21) 1936.

4. Maschkileisson, I.; Neradov, L., and Rapoport: Étude clinique et histologique de la leishmaniose cutanée boutonneuse (leishmaniose lupoïde), Ann. de dermat. et syph. **6**:229-241 (March) 1935.

5. Berlin, C.: Leishmaniasis Recidiva Cutis; Leishmanid, Arch. Dermat. & Syph. **41**:874-886 (May) 1940.

6. Smith, J. F.: Late Cutaneous Recurrence of South American Leishmaniasis After Treatment with Antimony, Brit. J. Dermat. **54**:231-234 (Aug.-Sept.) 1942.

of American leishmaniasis parasites are scarce or althogether indetectable. The same difficulty was encountered by Marchionini [7] in the atypical manifestations in cases of long standing. As a general rule, the demonstration of parasites seems to be particularly difficult in South American leishmaniasis. Garzon and Molina,[8] therefore, based their diagnoses on the clinical aspect, the differential diagnostic distinction from other lesions and the success of treatment with antimony and potassium tartrate, and it should be assumed that in these types the culture method would be of particular diagnostic significance.

Gitelzon [9] found among 3,197 cases 89 of "meta-leishmaniasis." Among our 600 cases of leishmaniasis, 62 were cases of recurrence, in which as a general rule smears contain no parasites, and to this number at least 10 per cent of the nodular and especially of the ulcerative early types should be added, in which it is impossible to detect the parasites even by repeatedly preparing smears. Behdjet [10] pointed out that in 4 per cent of his cases after healing had taken place tuberculous lesions appeared at the original site of the lesion. Probably he was dealing with recurrent leishmaniasis in which no parasites could be demonstrated, and the same applies to Sinderson.[11] The so-called lupus developing in leishmaniasis scars, according to these authors, probably would have been identified as a late leishmaniasis lesion if the appropriate culture method had been applied.

In view of the foregoing statements, it is all the more significant that in a number of dermatologic textbooks no mention is made of the culture method for diagnostic purposes (Sutton and Sutton,[12] Ormsby and Montgomery,[13] "Nouvelle pratique dermatologique," [14]

7. Marchionini, A.: Die Behandlung der Orientbeule (Hautleishmaniose), Schweiz. med. Wchnschr. **71**:1220-1223 (Oct. 18) 1941.

8. Garzon, R., and Molina, R. J.: A propósito de un caso de Leishmaniosis tegumentaria americana; consideraciones clinicas diagnósticas y terapéuticas, Rev. argent. dermatosif. **26**:225-247, 1942; cited by Wise, F., and Sulzberger, M. B.: 1942 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1942, p. 142.

9. Gitelzon, I. I.: (*a*) Atypical Forms of Cutaneous Leishmaniasis, Sovet. vestnik venerol. i dermat. **1**:34-36, 1932; (*b*) Skin Leishmaniasis, Ashkhabad, Turkmenistan Government, 1933; cited by Berlin.[5]

10. Behdjet, H.: A propos des boutons de Wright, in Deliberationes congressus dermatologorum internationale IX-1, Leipzig, Johann Ambrosius Barth, 1936, vol. 2, p. 598-605.

11. Sinderson, H. C.: Lupus Vulgaris and Oriental Sore, Tr. Roy. Soc. Trop. Med. & Hyg. **25**:75-76 (June) 1931.

12. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1943.

13. Ormsby, O. S. and Montgomery, H.: Diseases of the Skin, Philadelphia, Lea & Febiger, 1943.

14. Vigne, P.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 3.

etc.). Mayer and Nauck [15] wrote, in Jadassohn's Handbook, schematically that a diagnosis through culturing is only rarely deemed necessary, without entering on further details regarding that point.

In a few monographs only, dealing with tropical diseases, culturing is mentioned as a diagnostic method (Rogers,[16] Reed,[17] Manson-Bahr [18]). But even these authors failed to supply detailed information as to the significance of the method in the various types of the disease. The question seems to have gained great importance in this war, since the disease has spread considerably as a result of troop contingents passing through the Near East, and it is probable that atypical cases may turn up in nonendemic countries too, even after years. Recently Goldman,[19] in a review dealing with the preparation of the material for diagnostic purposes in various tropical dermatoses, described the technic of obtaining the material and emphasized the importance of the culture method for the diagnosis of leishmaniasis.

The few experiments outlined in the foregoing paragraphs seem to us to indicate that greater importance should be attached to the culture method for the diagnosis of leishmaniasis of endemic as well as of nonendemic spread than has so far been the case.

SUMMARY

The varied clinical picture of cutaneous leishmaniasis makes an objective diagnostic method a matter of greatest importance. Especially in the atypical and particularly in the late types of this disease, the microscopic demonstration of parasites often fails.

The results in 31 cases of leishmaniasis nodosa and leishmaniasis ulcerosa and in 30 cases of leishmaniasis recidiva have been used in evidence of the possibility that parasites can be demonstrated in cultures. In 26 cases the cultures were the only means of establishing the presence of parasites. Insufficient attention is being attached to this laboratory method as a diagnostic means in the textbooks on dermatology and, to some extent, in those dealing with tropical diseases.

Professor Adler and his assistant, Mr. Bar, of the Parasitological Institute of the Hebrew University, Jerusalem, Palestine, and Dr. Gurevitch, Head of the Bacteriological Institute of the Hadassah-Rothschild University Hospital, Jerusalem, Palestine, assisted with this paper.

15. Mayer, M. and Nauck, E. G.: Leishmaniosen der Haut und Schleimhaeute, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pt. 1.

16. Rogers, L., and Megaw, J. W. D.: Tropical Medicine, London, J. & A. Churchill, Ltd., 1930.

17. Reed, A. C.: Tropical Medicine in the United States, Philadelphia, J. B. Lippincott Company, 1930.

18. Manson-Bahr, P. H.: Manson's Tropical Diseases, London, Cassel & Co., Ltd., 1942.

19. Goldman, L.: Preparation of Material for Laboratory Diagnosis of Some Tropical Diseases of the Skin, Arch. Dermat. & Syph. **50**:264-266 (Oct.) 1944.

ASPERGILLUS INFECTION OF THE NAILS

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ASPERGILLI when found in mycologic cultures of the skin and of the nails have long been considered incidental clinic or laboratory contaminants and of no pathogenic significance. However, increasing evidence over the past twenty-five years has led to the realization that species of this genus of the fungi might actually be primary or secondary invaders of the human nail.[1] In 1941 one of us (E. S. B.) had the opportunity to investigate a case of primary invasion of the human nail by a species of Aspergillus. In this case each time nail scrapings were cultured they yielded large numbers of colonies of Aspergillus flavus, but no other species of fungus was recovered. It was observed in this case that the infected nail plate had a dull green discoloration in addition to the usual characteristics of onychomycosis, such as thickening, brittleness, vertical striations and crumbling of the distal portions. The organism on culture had a yellowish green color. It was therefore believed that the discoloration of the nail was caused by the abundant growth of the fungus in the heavily infected portions of the nail plate. A direct examination of the nail plate in a

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1. (*a*) Émile-Weil, P., and Gaudin, L.: Contribution à l'étude des onychomycoses: Onychomycoses a Penicillium, à Scopulariopsis, à Stérigmatocystis, à Spicaria, Arch. de méd. expér. et d'anat. path. **28**:452, 1919. (*b*) Sartory, A.: Sur un champignon nouveau du genre Aspergillus isolé dans un cas d'onychomycose, Compt. rend. Acad. d. sc. **170**:523, 1920. (*c*) Ota, M.: Sur une nouvelle espèce d' Aspergillus pathogène: Aspergillus jeanselmei n. sp., Ann. de parasitol. **1**:137, 1923. (*d*) Sartory, A.; Sartory, R.; Hufschmitt, G., and Meyer, J.: Un cas d'onychomycose provoquée par un Eurotium nouveau: Eurotium diplocyste n. sp., Compt. rend. Soc. de biol. **104**:881, 1930. (*e*) Smith, L. M.: Aspergillus Infection of the Nails, Urol. & Cutan. Rev. **38**:783, 1934. (*f*) Bereston, E. S., and Keil, H.: Onychomycosis Due to Aspergillus Flavus, Arch. Dermat. & Syph. **44**:420 (Sept.) 1941. (*g*) Rockwood, E. M.: A Study of Fungus-Infected Nails, ibid. **22**:395 (Sept.) 1930. (*h*) Bereston, E. S., and Warning, W. S.: Onychomycosis and Dermatomycosis caused by Trichophyton Rubrum and Aspergillus Nidulans, Arch. Dermat. & Syph. **52**:162, 1945.

10 per cent solution of potassium hydroxide revealed considerable hyphae and spores characteristic of Aspergillus. The organism obtained on cultures was identified by Dr. Charles Thom, leading authority on the Aspergilli, as A. flavus. Cultures of the organism were obtained repeatedly from many specimens of the infected toe nail. A photomicrograph of the strain A. flavus isolated in this case is shown in fig. 1.

Fig. 1.—Microscopic cultural appearance of Aspergillus flavus. *A* indicates the level of the surface. Just below the surface the hyphae are seen in abundance. *B* shows a conidiophore ending in a balloon-like vesicle, seen best at the point of the arrow. The circumference of the vesicle shows a single file of sterigmas, from which straight lines of spores or conidia issue (*C*).

Recently we reported a case of multiple infection of the finger nails and toe nails with Trichophyton rubrum and Aspergillus nidulans.[1h] In this case a number of specimens from the infected nails were obtained on seven different occasions during a period of two months. Culture of

these specimens produced T. rubrum in twelve culture tubes, A. nidulans in three tubes and both species in thirty-seven tubes. A. nidulans was isolated from every infected nail, which included both great toe nails and the index, middle and little finger nails of the left hand. Twelve specimens from the uninfected nails of this patient yielded no fungi of any species on culture. The characteristic green discoloration seen in the previously described case was again present in the nails in this second case, along with the usual signs of onychomycosis. A direct examination of numerous specimens of the infected nail plates in a 10 per cent solution of potassium hydroxide always revealed many hyphal elements.

In view of the aforementioned findings we have made an intensive search for other cases of this type during the past six months. Thirteen more cases of aspergillosis of the nail have been observed during this period. In all varying numbers of finger nails and toe nails were involved; a typical green discoloration was present; aspergillus growths were produced on culture, and hyphae or spores were revealed on direct microscopic examination. Six cases were followed completely, and in the other 7 the patients were examined as transient outpatients with no follow-up.

METHODS

Specimens of nail tissue were obtained, great care being taken against contamination. The feet were washed well with soap and water, followed by alcohol. The outer layers of the infected naills were then scraped away with a flamed scalpel, the inner brittle, crumbling portion being exposed. The scalpel was again flamed, and pieces of this inner portion were scraped directly into a sterile Petri dish, which was then covered immediately and sent to the laboratory. When received at the laboratory, the specimens were first inoculated into four routine agar slants: Sabouraud's dextrose, corn meal, wort and malt. The remaining particles of the nail were then examined microscopically, after being cleared with a 10 per cent potassium hydroxide solution.

The cultural and the microscopic data on the 6 cases which were followed are given in the table. The cultures of Aspergillus and Trichophyton obtained in these cases were sent to the Army Medical School in Washington, D. C., for confirmation of species. An additional 7 cases have been observed and the nails treated without complete laboratory follow-up. Primary cultures were made in them, however, with the isolation of Aspergillus glaucus in 4 and A. nidulans in 3 cases.

Culture of material taken from the nails in these cases presented a picture not found in cases in which there is no infection of the nails but in which accidental contamination has occurred. In a case of true infection all tubes inoculated begin to show colonies at the points of inoculation, as many as a dozen small gray colonies appearing on a single slant in about three days. Repeated specimens taken several months apart produce the same cultural picture. This type of multiple colony growth has been found only in the clinically typical cases of ungual infection. Of 1,732 culture tubes of fungous mediums inoculated with specimens of skin and nails during the past sixteen months, only 7 per cent have shown contamination due to Aspergillus. On numerous agar plates exposed as

Results of Microscopic and Cultural Examinations

Case	Date	Potassium Hydroxide Slide	Medium	Species Recovered
1	March 17, 1945	Positive	Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	March 17, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	March 27, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	March 27, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	April 23, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	April 23, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
2	April 12, 1945	Positive	Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	April 20, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	April 20, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
3	April 7, 1945	Positive	Sabouraud's	A. nidulans
			Corn meal	A. nidulans
			Wort agar	A. nidulans
			Malt agar	A. nidulans
	April 17, 1945		Sabouraud's	A. nidulans
			Corn meal	A. nidulans
			Wort agar	A. nidulans
			Malt agar	A. nidulans
4	April 10, 1945	Positive	Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
	April 17, 1945		Sabouraud's	A. glaucus
			Corn meal	A. glaucus
			Wort agar	A. glaucus
			Malt agar	A. glaucus
5	Dec. 28, 1944	Positive	Sabouraud's	A. glaucus and T. rubrum
			Corn meal	A. glaucus and T. rubrum
			Wort agar	A. glaucus and T. rubrum
			Malt agar	A. glaucus and T. rubrum
	April 26, 1945		Sabouraud's	A. glaucus and T. rubrum
			Corn meal	A. glaucus and T. rubrum
			Wort agar	A. glaucus and T. rubrum
			Malt agar	A. glaucus and T. rubrum
6	Feb. 19, 1945	Positive	Sabouraud's	A. glaucus and T. rubrum
			Corn meal	A. glaucus and T. rubrum
			Wort agar	A. glaucus and T. rubrum
			Malt agar	A. glaucus and T. rubrum
	March 3, 1945		Sabouraud's	A. glaucus and T. rubrum
			Corn meal	A. glaucus and T. rubrum
			Wort agar	A. glaucus and T. rubrum
			Malt agar	A. glaucus and T. rubrum

checks in the laboratory there grew only an occasional colony of Aspergillus. In the laboratory fungous contamination has been kept to a minimum by using only tubed mediums as a routine and by forbidding the opening of mature cultures of fungi in the bacteriology section.

COMMENT

The clearcut cultural findings in our cases of onychomycosis due to Aspergillus, coupled with the gross physical characteristics, leave no doubt that this disease is a clinical entity. We have never observed the typical green discoloration seen in aspergillosis of the nails in any of our cases of proved onychomycosis due to other fungi.

Fig. 2.—Onychomycosis due to infection with Aspergillus.

In view of our observations it is our opinion that onychomycosis can be caused primarily by the following species of Aspergillus: A. nidulans, A. glaucus and A. flavus. Multiple infection of the nails with one of these species of Aspergillus and T. rubrum can also occur.

The clinical picture of aspergillosis of the nail is as follows: thickening, brittleness, greenish or yellowish discoloration, vertical striations and crumbling of the distal portions of the infected nail (fig. 2). The

treatment in all cases of onychomycosis is highly unsatisfactory at present because avulsion of the nail plates, roentgen ray therapy, application of fungicidal drugs and repeated scraping of the nail have not helped in any of our cases or in others of which we have knowledge. It is hoped that by the light being shed on the cause of onychomycosis new and effective methods of therapy may be developed.

SUMMARY

A careful mycologic study of 13 cases of onychomycosis disclosed that Aspergillus glaucus or Aspergillus nidulans can cause this disease whether present alone or occurring in conjunction with Trichophyton rubrum. Repeated cultures in 6 cases disclosed that in 3 the disease was caused by A. glaucus, in 1 by A. nidulans and in 2 by double infection with A. glaucus and T. rubrum. Seven additional cases were observed, in which cultures were made once. In these the disease was found to be caused by A. glaucus or A. nidulans. In the 13 cases there were all the usual characteristics of other forms of fungous infection of the nail in addition to a typical greenish discoloration of the nail plate. Evidence is presented to show that the species of Aspergillus culture in these cases cannot be considered accidental clinical or laboratory contaminations but were actually present in the infected nails in considerable quantity. It is therefore postulated that the nails of the fingers or the toes of human beings may be invaded by some species of Aspergillus, with production of a pathologic condition resembling the onychomycoses produced by other fungi.

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Coral Gables, Fla.

DERMATOPHYTOSIS DUE TO COMBINED INFECTION WITH TRICHOPHYTON INTERDIGITALE AND TRICHOPHYTON PURPUREUM

Report of a Case

EMANUEL MUSKATBLIT, M.D.
NEW YORK

A WHITE woman aged 42 gave a history of an itchy eruption of four months' duration on the left foot, which was rapidly followed by an eruption on each hand. The examination revealed minute deep-seated intraepidermal vesicles on the fingers of both hands and on the left palm, without a noticeable inflammatory reaction. On the left sole there was a vesicular eruption, with erythema and scaling. Scrapings from the fingers revealed no fungi in a potassium hydroxide preparation; scrapings from the left sole showed fungous filaments and chains of spores. This was, therefore, a case of dermatophytosis of the left sole. The eruption on the hands could be considered a dermatophytid because of its clinical features and the lack of contact with possible cutaneous irritants. Cultures made on Sabouraud's medium (dextrose-peptone-agar) with material taken from the left sole produced a curious combination of colonies of two different types, growing side by side in the same culture tubes. The one, identified as a colony of Trichophyton interdigitale, was white and downy, with irregular grooves, folds and convolutions. The other, identified as a colony of Trichophyton purpureum, showed an elevated center covered with pinkish down, a flat, yellow and powdery middle zone and a peripheral fringe of submerged rays, powdery on the surface and deep red on transillumination. Later on this culture was completely covered with a pink down. Culture mounts of both fungi presented identical forms of sporulation, namely, numerous small conidia (aleurospores) on simple and branched filaments and chlamydospores. Neither spiral coils nor fuseaux were found. The identification of the two different species was based on different gross appearance, especially on the presence of red pigment in the surface down and in the basal layer of colonies classified as T. purpureum. In treatment a 5 per cent solution of salicylic acid in alcohol was applied on the foot once daily and a zinc oxide–talcum lotion on the hands. Four fractional doses of roentgen rays (75 r) were also given at weekly intervals. Four months later the patient was free from any symptoms or signs of her disease. Scrapings from the left sole yielded no fungi.

This case is interesting not only as a mycologic curiosity with two different fungi on cultures. Both species, T. interdigitale and T. purpureum, were isolated from a vesicular eruption. T. purpureum usually causes dry, scaly, infiltrated and lichenified lesions. T. interdigitale often produces vesicular eruptions. This case presented clinical features common for T. interdigitale. The other partner of this fungous symbiosis, T. purpureum, did not show its clinical characteristics. The same was true in regard to the results of the therapy. Lesions pro-

duced by T. purpureum are noted for their resistance to treatment. In this case a mild type of treatment cleared the eruption clinically and microscopically. The presence of an eruption on the hands typical for a dermatophytid is a feature common in diseases due to T. interdigitale and practically unknown in T. purpureum infections.

It is possible that T. interdigitale acted as an antagonist of T. purpureum and inhibited the latter's vitality. It is also possible that T. interdigitale stimulated the immunologic response of the skin and thereby contributed to the cure. T. purpureum is known as a poor

Trichophyton interdigitale (left) and Trichophyton purpureum (right) isolated from a case of dermatophytosis of the foot.

sensitizer, a fact which explains at least partially the poor therapeutic results. Whatever the cause, it was a symbiosis of two pathogenic fungi in which one of them played the predominant part, determining the clinical picture and the course of the disease, while the other behaved more like an innocuous saprophyte.

The interesting question whether an artificial inoculation of T. interdigitale into the skin of a patient with lesions due to T. purpureum will increase the immunologic response and speed up the cure can be answered only by experimentation.

55 West Forty-Second Street.

ERYTHEMA MULTIFORME AND ERYTHEMA NODOSUM

A Comparative Study of Fifty-Four Patients

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AND
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NOT ALL the etiologic factors involved in the causation of erythema multiforme are as yet clear. It is also true that in the therapeusis of this dermatosis success is occasionally difficult to obtain. Because of these facts, an analytic study was made of 40 unselected patients having typical erythema multiforme exudativum. Six of these patients had accompanying bullous lesions. In view of the close relationship between erythema multiforme and erythema nodosum, 14 additional patients with the latter disease were also studied for comparison. Examples of both types of lesions were not exhibited by any one patient in this study.

The 54 patients were examined carefully, and every attempt was made to evaluate thoroughly the background, the history, the physical findings and the accessory clinical findings in each patient. In addition to inquiry being directed to age, sex, race, temperature, systemic symptoms, family history, season of incidence, occupation, duration of disease and characteristics of lesions, special attention was paid to foci of infection, laboratory findings in the peripheral blood, urinalyses, roentgenograms, condition of the nose and the throat, bacteriologic cultures, intradermal tests, presence or absence of nervous tension and response to various types of therapy.

In table 1 are listed the average age of the patients, their distribution as regards sex and the duration of the lesions in both groups. It is significant that among the 54 unselected members of the two erythema groups not one was a Negro, although there is seen 1 Negro patient for every 3 white patients in the medical clinics of Duke Hospital. The known greater frequency of occurrence of erythema nodosum in females is substantiated, whereas in patients with erythema multiforme the sexes tend to be more evenly represented. In adults the age of incidence, although variable, was most commonly the fourth decade. No patients of pediatric age were included in this study. Most of the patients had their disease less than four weeks.

From the Division of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine, Durham, N. C.

Certain factors were found to be inconsistent and apparently of little significance with reference to etiologic considerations, namely, occupation and family and past histories, with particular emphasis being given to tuberculosis, allergic diseases, nervous tension or other familial influences.

Table 2 demonstrates the tendency of the incidence to increase during the spring and fall seasons, which has long been recognized.[1] It would seem difficult to appreciate this definite seasonal variation unless one could assume that it is closely related to other factors.

TABLE 1.—*Average Age, Race and Sex of Patients and Duration of Lesions*

Disease	No. of Patients	Average Age	Race		Sex		Duration of Lesion		
			White	Negro	Male	Female	1 Mo.	6 Mo.	1Yr.
Erythema multiforme	40	39	40	0	21	19	37	2	1
Erythema nodosum	14	30	14	0	3	11	13	1	0

Guy [1a] originally reported an epidemic of erythema multiforme occurring during February and March 1918 in 47 patients. Hemolytic streptococci were isolated in cultures of material from either the throat or the vaccination wounds of 32 of these patients. In addition, 9 patients harbored pyogenic streptococci in their throats. Spink [1b] has pointed out the similarity between the curves of incidence of erythema nodosum and known streptococcic infection in 95 patients with acute follicular tonsillitis, from each of whom beta hemolytic streptococci

TABLE 2.—*Monthly Incidence of Erythema Multiforme and Erythema Nodosum*

Disease	No. of Patients	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Erythema multiforme	40	1	7	3	6	4	0	2	4	3	6	4	0
Erythema nodosum	14	3	1	1	2	3	2	0	1	0	1	0	0

were isolated. The seasonal incidence of the common cold as determined by Kler,[2] however, does not coincide precisely with the seasonal occurrence of erythema multiforme and erythema nodosum. Thus, the possible relationship between common infections of the upper part of the respiratory tract and these two erythemas warrants further study.

1. (*a*) Guy, W. H.: Erythema Multiforme: A Clinical and Laboratory Study of Forty-Seven Cases, J. A. M. A. **71**:1993 (Dec. 14) 1918. (*b*) Spink, W. W.: Pathogenesis of Erythema Nodosum, with Special Reference to Tuberculosis, Streptococcic Infection and Rheumatic Fever, Arch. Int. Med. **59**:65 (Jan.) 1937.

2. Kler, J. H.: An Analysis of Colds in Industry, Arch. Otolaryng. **41**: 395 (June) 1945.

The systemic signs and symptoms which accompany erythema multiforme and erythema nodosum emphasize the systemic nature of the two diseases. Table 3 lists the more commonly occurring systemic signs and symptoms in the order of their frequency. Fever and generalized malaise were most often present.

In table 4 are listed the average results of numerous laboratory determinations in both groups. The normality of the color indexes and

TABLE 3.—*Common Noncutaneous Signs and Symptoms of Erythema Multiforme and Erythema Nodosum*

Disease	No. of Patients	Fever	Malaise	Cough	Arthralgia	Nausea and Emesis
Erythema multiforme	40	14	8	8	5	2
Erythema nodosum	14	7	6	3	5	2

of the differential leukocyte counts is apparent. The slightly lower hemoglobin determinations of the erythema nodosum group may have been due to the fact that most of these patients were women. Corrected sedimentation rates were consistently elevated above the upper limit of normal. Slightly elevated leukocyte counts were usually present,

TABLE 4.—*Average Accessory Clinical Determinations in Cases of Erythema Multiforme and Erythema Nodosum*

	Disease	
	Erythema Multiforme	Erythema Nodosum
Number of patients	40	14
Hemoglobin, Gm. (Sahli)	13.6	12.4
Color index	0.98	0.95
Corrected sedimentation rate	28	26
Weltmann coagulation band (normal 6)	4	5
Leukocyte count	10,070	11,870
Differential leukocyte count	Per Cent	Per Cent
Polymorphonuclears		
Segmented forms	63	65
Staff forms	5	5
Juvenile forms	1	1
Basophils	1	0
Eosinophils	3	1
Monocytes	5	6
Large lymphocytes	7	3
Small lymphocytes	15	19

and only one count was below 5,000. Consistent eosinophilia was not a feature. The Weltmann coagulation band averaged 4 in the erythema multiforme group and 5 in the erythema nodosum group, indicating that in both instances exudative pathologic processes were present.[3]

3. Dees, S. C.: The Weltmann Reaction in Bronchial Asthma, J. Allergy **14**:469 (Sept.) 1943.

A decided effort was made to check each patient for foci of infection, and it was interesting to find that 45 of the 54 patients had definite evidences of infection. It is recognized that the significance of this observation is open to question. As shown in table 5, the roentgenologic evidences of infection were found frequently to involve, in the order named, the chest, the sinuses and the teeth. Kerley [4] found evidence of recent intrathoracic disease by roentgenologic examination in 28 of 37 patients with erythema nodosum. The average age in his group was 21 years. This lower average age may possibly account for the greater

TABLE 5.—*Incidence of Infection in Patients with Erythema Multiforme and Erythema Nodosum as Demonstrated by Roentgenologic and Otolaryngologic Study*

	Otolaryngologic Examination			Roentgenologic Examination: Sinus		Chest		Teeth	
Disease	Tonsillitis	Sinusitis	Normal	Infection Present	Normal	Infection Present	Normal	Infection Present	Normal
Erythema multiforme	8	7	1	7	22	11	24	6	17
Erythema nodosum	6	1	1	1	9	5	8	1	4

TABLE 6.—*Incidence of Cultured Organisms in Patients with Erythema Multiforme and Erythema Nodosum*

	Disease	
	Erythema Multiforme	Erythema Nodosum
Cultures of material from nose and throat or of sputum		
Str. viridans	15	6
Str. pyogenes	1	0
Staph. aureus (hemolytic)	9	0
Staph. aureus	3	1
Negative	6	1
Cultures of stool		
Hemolytic organisms	7	1
Negative	0	0
Cultures of urine		
Staph. aureus	2	2
Negative	3	1

incidence of recent pulmonary disease in his group. An examination by an otolaryngologist also revealed in some patients tonsillitis, pharyngitis or sinusitis. The figures are also shown in table 5. All patients who appeared on routine examination to have probable disease of the upper part of the respiratory tract were referred to an otolaryngologist.

Table 6 discloses the types of organisms isolated from the nose and the throat and from the sputum, the urine and the stools. Alpha hemolytic streptococci (Streptococcus viridans) were found to be present most frequently.

4. Kerley, P.: The Etiology of Erythema Nodosum, Brit. J. Radiol. **16**:199 (July) 1943.

Of 17 female patients who had pelvic examinations, 8 were found to have chronic cervicitis or evidence of other pelvic inflammatory disease. Four of these 8 patients had erythema nodosum and 4 had erythema multiforme.

Of 9 patients without obvious evidence of infection, only 1 gave a history of possible drug sensitivity and of taking the suspected drug prior to the outbreak of his cutaneous eruption. This particular patient was the only one, in the entire number of 54 patients, who by history could fairly definitely be said to have a dermal reaction probably attributable to drug sensitivity. Only 18 of the 54 patients gave a history of taking any drug during the four weeks prior to the onset of their disease. Ten of the 18 patients had been taking one of the sulfonamide compounds, and the other patients had been taking proprietary preparations. Of the 10 patients receiving sulfonamide compounds prior to the study, 2 again were given sulfonamide drugs without exacerbation of their eruption. By history, one suspects that drugs played an insignificant causative role in the eruptions of these 54 patients.

Five of 12 patients were sensitive to staphylococcus toxoid by intradermal testing. Similarly, 6 of 15 patients were sensitive to one or more of the streptococcic allergens. Ten patients were tested intradermally with the various food allergens and pollens. In 4 of these the tests elicited no reactions at all, whereas in the remaining 6 the tests elicited one or more positive reactions. These results, however, could not be correlated by history with the cause of the disease.

Of 8 patients with erythema multiforme in whom studies of vitamin levels were undertaken, all were found to have adequate plasma levels of vitamins C and A and carotene.[5]

The average patient was free of his disease within four weeks after the onset, apparently regardless of the nature of the therapy administered. Definitely, those patients with erythema nodosum, which involved most commonly and most intensively the lower extremities, responded much more rapidly when they were put to bed with their legs elevated. Generally the same can be said for rest in bed as regards the patients with erythema multiforme.

Of 40 patients with erythema multiforme, all but 2 were hospitalized for investigation and treatment. Of the 38 patients hospitalized, 36 (95 per cent) were well within four weeks from the time of the onset of their disease and had no recurrences for at least six months after their recovery. Their treatment could be divided essentially into two types: (1) medical (28 patients), which included the administration of one or any combination of salicylates, sulfonamide compounds, penicillin, vaccine (for desensitization) or roentgen rays; (2) primarily

5. Callaway, J. L.; Milam, D. F., and Noojin, R. O.: Nutritional Survey of 354 Dermatologic Patients, Arch. Dermat. & Syph. **51**:266 (April) 1945.

surgical (10 patients), which included tonsillectomy and adenoidectomy or removal of abscessed teeth. Regardless of whether the patient was treated in the hospital primarily medically or surgically, the average patient became well in less than four weeks from the time of the onset of his disease.

The erythema nodosum group responded similarly. Rest in bed, with elevation of the lower extremities, was noted significantly to be desirable for patients with erythema nodosum who had lesions on their lower extremities. In 1 patient frank pulmonary tuberculosis developed within eight months after the onset of erythema nodosum. At the time the erythema nodosum was present, a roentgen film showed the chest was normal.

SUMMARY AND CONCLUSIONS

An analytic and comparative study has been made of 40 patients with erythema multiforme and 14 patients with erythema nodosum.

Both diseases appear to be less common among Negroes.

Except for the clinical appearance, the sex incidence and the possible relationship of tuberculosis, erythema multiforme and erythema nodosum are remarkably alike in many of their manifestations.

The fourth decade held the largest adult age group for both diseases.

Fever and generalized malaise most often accompanied the cutaneous manifestations.

Laboratory examination disclosed consistently a normal color index, a normal differential leukocyte count without eosinophilia, an elevated sedimentation rate, a slightly elevated total peripheral blood leukocyte count and a Weltmann coagulation band of less than 6.

Forty-five of the 54 patients had one or more evidences of focal infection.

A streptococcus was isolated from these patients more frequently than any other organism.

Drug sensitivity apparently was of little significance in either group in the causation of disease.

Intradermal tests in general did not significantly contribute to the management of either disease.

Most patients were free of their disease within four weeks of the onset, regardless of the nature of the therapy administered.

Mrs. Jane Stitt and Mrs. Judy Gadsden gave helpful assistance in the collection and the analysis of the material presented.

Clinical Notes

PROGRESSIVE SYPHILITIC OPTIC ATROPHY BENEFITED BY COMBINED PENICILLIN AND FEVER THERAPY

Report of a Case

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In Collaboration with J. H. BARR, M.D.
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THE DRAMATIC improvement in vision achieved by the combined use of penicillin and fever therapy in a case of advancing syphilitic optic atrophy prompts this report.

S. M., a white man aged 34, noticed dimness of vision in the left eye late in November 1944. At the beginning, this blurring was inconstant and limited to "the inside, near my nose." Gradually this disturbance became constant and more extensive until, finally, all the vision was gone. When the patient consulted Dr. W. E. Bruner in January 1945, there was total blindness of the left eye. Dr. Bruner found pallor of the nerve head on the left side and also Argyll-Robertson pupils.

S. M. was referred to me by Dr. Bruner and was examined on Feb. 1, 1945. At the initial visit he had total blindness in the left eye and rather casually mentioned some visual difficulty with the right eye as well. Every so often a watery film seemed to cover objects at which he looked. Examination showed myotic pupils which did not react to light but did constrict on accommodation. The left disk was pale white and its margins sharply circumscribed. The right disk was slightly pale.

Except for the eyes, all the functions of the cranial nerve were intact. The results of neuromuscular examination and the sensory tests were normal. Mentally, the patient was of average intelligence, his emotional state was normal and he was cooperative in every way. Unusual was his apparent indifference to the failing vision and his delay in seeking help. As regards past history, he mentioned that at the age of 15 he had a penile lesion, which was treated locally and then neglected.

S. M. was placed in the University Hospitals for further study and treatment. The Kline reaction of the blood was positive. The spinal fluid was under normal pressure, the cell count revealed 33 lymphocytes, the total protein level was 28.5 mg. per hundred cubic centimeters and the Wassermann reaction was positive in dilutions of 0.5 and 1 cc. The colloidal gum mastic curve was 3322100000. Results of the remainder of the laboratory tests and the physical examination were normal.

At the time of hospitalization, visual field studies showed a slight constriction in the right field. There had been additional loss of visual acuity since the initial examination in my office. The patient voluntarily stated that he could no longer read the comics but was still able to read the headlines of the daily newspaper.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Western Reserve University School of Medicine.

Even the reading of large print required determined effort, and the page seemed blurred by a watery sheen. At this time the disk was more pale than several days previously.

Because of the rapidly advancing optic atrophy, fever therapy was started immediately, typhoid vaccine being used intravenously while the spontaneous paroxysms from a malarial inoculation were awaited. The patient was allowed to have eleven paroxysms in all, seven with typhoid vaccine and four with malaria, for a total of forty-four and a half hours, above 40 C. (104 F.). Simultaneously with fever therapy, penicillin was administered. The patient was given 25,000 units of penicillin intramuscularly every three hours, for a total of 4,000,000 units in twenty days.

At the end of the first week, during which he had several chills and was given over 1,000,000 units of penicillin, the patient stated that he could see more clearly. He could now read the headlines of the newspaper more readily. There was additional improvement during the second week. When the treatment was completed, the patient was able to read the fine print of his favorite comic page and the watery sheen was gone.

S. M. was discharged early in March 1945, and his progress was followed thereafter. In the middle of March, the vision was tested with the rating reading card of the American Medical Association. The patient was able to read with his right eye the smaller letters at a distance of 14 inches (35.5 cm.), the rating being 56.5 per cent of normal. Toward the end of March, he was able to read the finest print, with a rating of 100 per cent. However, the color of the disk was still distinctly pale. Throughout the period of observation, the left eye remained totally blind and the disk white.

Early in April, the patient resumed his occupation as a machinist and was able to handle his tools skilfully. At this time he could see perfectly well out of the right eye and could read the finest print as long as he wished, without any fatigue. Acuity for near and distant vision was roughly normal. A reexamination in June 1945 (one hundred and nine days after onset of therapy) revealed satisfactory vision in the right eye and improvement in the spinal fluid: The colloidal gum mastic curve was normal; the Wassermann reaction with 0.1 cc. was negative, with 0.5 cc. 4 plus and with 1 cc. 4 plus; the cell count was 2 lymphocytes, and the total protein level was 34 mg. per hundred cubic centimeters.

COMMENT

Syphilitic optic atrophy is one of the most serious manifestations of syphilis. In my experience, when the vision in one eye is gone and in the other is dim, the course is usually a downward one. Moore [1] stressed the poor prognosis in any patient with loss of vision in one eye and progressive changes in the other. Consequently, physicians who saw S. M. on his admission to the hospital had a feeling of hopelessness. For this reason it was decided not to rely on fever therapy alone but to use penicillin also. This decision to use penicillin depended on its proved success in treatment of early syphilis. There is a favorable clinical report by Stokes and colleagues,[2] who had had good results with penicillin in cases of ocular

1. Moore, J. E.; Kemp, J. E., and others: The Modern Treatment of Syphilis, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1941.

2. Stokes, J. H.; Sternberg, T. H.; Schwartz, W. H.; Mahoney, J. F.; Moore, J. E., and Woods, W. B., Jr.: The Action of Penicillin in Late Syphilis, J. A. M. A. **126**:73 (Sept. 9) 1944.

syphilis. "In ocular syphilis, simple inflammatory processes respond; later and more complicated lesions such as the optic neuritides and interstitial keratitis recover, relapse, present resistance and residues proportional to damage already done."

The therapeutic result obtained in the case reported was distinctly superior to the improvement in several cases reported by Stokes and his co-workers[3] in which penicillin alone was used. These investigators concluded: "Penicillin alone may favorably affect any type of active neurosyphilis; symptomatic and asymptomatic. . . . It may arrest progression in primary optic atrophy with short observation; has thus far blinded no one; may produce slight improvement in vision and fields; may return the spinal fluid to normal, including Type III; may fail (in lower dosage) to stop a localized chiasm lesion, despite such spinal fluid improvement."

SUMMARY

A case of syphilitic optic atrophy is reported in which there was total blindness in one eye and progressive loss of vision in the other eye, with pallor of the nerve head. Treatment with combined fever and penicillin was instituted. The condition of the blind eye remained unchanged, but almost normal vision was restored to the other eye. However, eighteen months after the apparent recovery, the visual acuity decreased. Further treatment has been instituted.

Dr. W. E. Bruner and Dr. A. B. Bruner checked the patient's visual status from time to time, and the Department of Dermatology and Syphilology, Dr. H. N. Cole, Director, furnished the penicillin and the dosage outlined.

3. Stokes, J. H., and others: Penicillin in Late Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **29**:313 (May) 1945.

BIOPSY GUIDE

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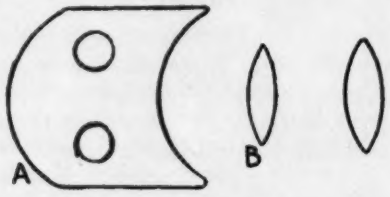
The removal of a specimen for biopsy may be facilitated by the use of a flat metal guide, convex on one border and concave on the other. The first incision may be made along the convex border to the desired extent and the ellipse



A, guide; *B*, incisions of two sizes.

completed by turning the guide and cutting along the concave border. If it is preferred, the concave border may be used for both incisions.

Correspondence

DOSAGE IN TOPICAL THERAPY

To the Editor:—The report of Dr. Herman Goodman in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, July 1946, page 62, is highly provocative in that it brings into sharp focus our understanding of dosage in topical therapy for the skin. Essentially, the establishment of effective dosage of an active drug involves maintenance of a proper concentration of the drug in the tissue concerned. And so, for internal therapy, dosage is based on body weight, and exhibition of the drug is repeated at proper intervals to keep adequate its concentration in the organism over the required period. For topical treatment the same principles operate except that surface area is substituted for body weight in estimating the anticipated concentration of the drug in skin, for the skin covered by the medicament is accepted as the only area of skin receiving therapy.

Vehicles for topical drugs serve the purpose, among others, of making possible the even distribution of the drug over the whole unit of cutaneous area treated. Thus, if it is assumed that 1 Gm. of a grease base mixture is to be spread over 4 square inches (25.8 sq. cm.) of skin, a 1 per cent salve of salicylic acid in this vehicle would supply 10 mg. of the acid evenly dispersed over these 4 square inches. No matter what the character of the vehicle, if 1 Gm. of the medicated salve contained 10 mg. of drug and the vehicle permits a spreading of the drug evenly over the 4 square inches, the dosage offered the skin remains identical, independent of what happens to the vehicle thereafter (evaporation from the cutaneous surface, etc.).

Dr. Goodman does not believe that this is so. His explanation as to why this is not so reveals an unusual understanding of topical dosage.

To quote Dr. Goodman:

"Chrysarobin is prescribed in a medium of chloroform . . . prescriptions . . . disclose great variation in the percentage of chrysarobin ordered. The evaporation of the chloroform from the skin at the time of application levels all distinction as to percentage of chrysarobin. The film on the skin is 100 per cent chrysarobin."

Levels all distinction indeed! Yes, the film on the skin is 100 per cent chrysarobin but 1 cc. of a 1 per cent solution is 10 mg. of film of chrysarobin; 1 cc. of a 5 per cent solution is 50 mg. of film of chrysarobin; both are 100 per cent films of chrysarobin, but what of the quantity of drug in each film?

HERMAN SHARLIT, M.D., New York.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

LYMPHOGRANULOMA VENEREUM. F. C. COMBES, O. CANIZARES and S. LANDY, Am. J. Syph., Gonor. & Ven. Dis. **29**:611 (Nov.) 1945.

The authors report on the result of the formaldehyde-gel test and the serum albumin-globulin ratio as determined in 42 cases of lymphogranuloma venereum. In 38, or 90.5 per cent, the result of the test was positive and the serum showed hyperglobulinemia. In 15 cases, followed for a period of sixteen weeks, there was a decided tendency for the result of the test to return to normal after clinical cure.

The formaldehyde-gel test is a simple reliable bedside procedure by which to determine the presence of hyperglobulinemia in patients with lymphogranuloma venereum. The result of this test and the albumin-globulin ratio should be used as aids in treatment and as indications of biologic cure in all cases of lymphogranuloma venereum.

STUDIES ON CHANCROID. PAUL B. BEESON and ALBERT HEYMAN, Am. J. Syph., Gonor. & Ven. Dis. **29**:633 (Nov.) 1945.

Because culture of material taken from a lesion suspected to contain the Ducrey bacillus as a means of diagnosis of chancroid has generally been abandoned as impracticable, the authors report in detail the technical method which has given them the best results. While an exact statement of the efficiency of diagnosis by culture could not be made, it seemed probable that a diagnosis can be made by culture in at least 75 per cent of all cases of chancroid. In pure culture the Ducrey bacillus grows well on mediums containing a body fluid, such as blood or serum. The medium which gave the best results was defibrinated rabbit blood. A technical detail of importance is the use of a very small inoculum from the genital lesion. The morphologic aspects and the staining of the Ducrey bacillus are sufficiently characteristic to permit a reasonably certain diagnosis based only on an examination of stained smears from the rabbit blood cultures.

CARDIOLIPIN ANTIGENS IN THE SERODIAGNOSIS OF SYPHILIS. CHARLES R. REIN and HILFRED N. BOSSAK, Am. J. Syph., Gonor. & Ven. Dis. **30**:40 (Jan.) 1946.

Cardiolipin antigen, composed of cardiolipin (0.2 per cent), a substance isolated from beef heart, and lecithin (1.3 per cent), was successfully adapted for use in a microflocculation slide test for syphilis. The sensitivity of the microflocculation slide test made with this antigen was higher than that observed with Kline diagnostic, Mazzini, Kahn and Kolmer tests performed in the authors' laboratory. The cardiolipin antigen showed extraordinary specificity in the presence of malarial infection. Such specificity was not evident when the serums tested were from patients with leprosy and infectious mononucleosis.

THE RELATIVE PROPHYLACTIC EFFECTIVENESS AGAINST SYPHILIS OF OINTMENTS CONTAINING CALOMEL IN DIFFERENT PARTICLE SIZE. WILLIAM L. FLEMING and MARY H. WOLF, Am. J. Syph., Gonor. & Ven. Dis. **30**:47 (Jan.) 1946.

The authors carried out an experiment with rabbits to evaluate the effect of the particle size of mild mercurous chloride on the efficacy of ointment of mild mercurous chloride as used in prophylaxis of syphilis. Three different ointments

containing mild mercurous chloride in 100 micron, 5 micron and 1 micron particle size were used.

Much greater protection was obtained with the ointments containing the smaller particles, that containing the 100 micron particles being relatively ineffective. The amount of ointment used seemed to play little part in the results, although the larger dose did afford somewhat better protection than the smaller. The results also seemed to give some indication that the local action of mild mercurous chloride was more important than the systemic.

Syphilitic Vascular or Cardiovascular Disease Occurring in Early Adult Life Following Acquired Syphilitic Infection. I. L. Schamberg, Am. J. Syph., Gonor. & Ven. Dis. **30**:58 (Jan.) 1946.

Five patients were presented, in whom serious syphilitic lesions of the vascular or cardiovascular organs developed in early adult life. In 3 the interval between the early lesions of syphilis and the first symptoms of vascular disease was two, thirteen and fifteen years, respectively. No conclusions could be drawn as to what effect the age at which syphilis is acquired has on the rapidity of progression of syphilitic vascular disease.

Studies on Liver Function. Ewart Hinds and Frederick Kalz, Am. J. Syph., Gonor. & Ven. Dis. **30**:70 (Jan.) 1946.

Greatly impaired hepatic function and significantly reduced prothrombin concentration indicate arsenical toxicity. In such cases therapy should be stopped at once. Two fatal cases of toxic encephalopathy are reported. In 1 case death occurred after a total dose of 240 mg. of oxophenarsine hydrochloride (mapharsen). In the other case death occurred after a total dose of 720 mg. of the drug had been given. Because of the inability to predict or to prevent arsenical encephalopathy and because in some patients small doses of arsenicals cause fatal reactions and discontinuation of arsenotherapy does not necessarily prevent the development of serious and sometimes fatal sequelae, the authors feel that massive arsenotherapy should be abolished.

Reuter, Milwaukee.

Reversal of Lingual Atrophic Changes with Nicotinamide Therapy. Elmer L. Sevringhaus and Emma D. Kyhos, Arch. Int. Med. **76**:31 (July) 1945.

As evidence of nicotinic acid deficiency Kruse described lingual fissures, atrophy of filiform papillae and dental scalloping of the margin of the tongue. Sevringhaus and Kyhos found such changes in 30 of 102 prison inmates. Of 17 men with fissured tongues 14 made significant improvement after taking 50 mg. of nicotinamide daily for not more than nineteen weeks. Five men received treatment because of marginal changes, which responded in 3 instances. It was found difficult to gage improvement in the condition of the papillae, but the authors were satisfied that these changes responded better than did the others. It is concluded that the criteria of chronic aniacinamidosis proposed by Kruse are valid.

Similar changes were noted in 3 anemic patients, whose conditions likewise improved promptly.

Esophageal Lesions Associated with Acrosclerosis and Scleroderma. Arthur M. Olsen, Paul A. O'Leary and B. R. Kirklin, Arch. Int. Med. **76**:189 (Oct.) 1945.

After reviewing previous reports of 32 cases in which scleroderma was accompanied with esophageal lesions, Olsen, O'Leary and Kirklin analyzed the records of 350 patients with scleroderma or acrosclerosis, after finding dysphagia or esophageal lesions in 36. Their study is concerned chiefly with 18 cases in which conclusive roentgenographic or endoscopic observations were made. In all these cases the symptoms of Raynaud's syndrome preceded or were coincident with

the development of cutaneous manifestations. (In 15 of the remaining 18 cases the diagnosis was also acrosclerosis.) The cases are reported individually, and the roentgenologic and endoscopic changes are described in detail.

The vasomotor phenomena and, in most instances, the sclerodermatous changes preceded the dysphagia or substernal burning, and the esophageal disturbance was most often a delayed manifestation of the disease. The authors state that when the esophageal difficulties are obstructive, temporary relief can be obtained almost invariably by dilation of the esophagus with sounds over a previously swallowed thread. In cases of cardiospasm associated with acrosclerosis or scleroderma, hydrostatic dilatation is not advisable. Sometimes the passage of the esophagoscope alone is enough to relieve the dysphagia. It is not advisable to use sounds larger than the no. 45 French sound in dilating organic lesions of the esophagus. Frequently, a repeated passage of sounds is necessary to maintain an adequate esophageal lumen.

CANCER IN RELATION TO USAGES: THREE NEW TYPES IN INDIA. V. R. KHANOLKAR and B. SURYABAI, Arch. Path. **40**:351 (Nov.-Dec.) 1945.

The authors had occasion to study, in different parts of India, three types of cancer which they believe may be attributed to certain usages prevalent in those regions. In 9 cases of "dhoti cancer" there was squamous cell cancer of the trunk, and the location was along the lines of the greatest friction or pressure of the garment (dhoti). The nature of the garment is such that it subjects to the greatest friction those sites of the body which are often soiled with dust and sweat and have the least opportunity of a thorough cleansing.

In certain provinces the natives habitually smoke a local type of cigar, called the chutta, with its burning end inside the mouth. Leukoplakic lesions of the hard palate were frequently observed among chutta smokers. There is frequent supervention of carcinoma of a serious type. The increased incidence is indicated by the fact that in one province palatal carcinoma was almost six times as frequent as carcinoma of the tongue.

Khaini, a mixture of a powder of dried tobacco leaf with lime, is deposited in the groove between the front teeth and the lower lip. It is left there until it is gradually diluted with saliva and is then swallowed. This procedure appears to result frequently in carcinoma of the mouth.

In the first and second instances the authors discuss the histologic changes of the carcinoma and the apparently precancerous processes. The implications are also thoroughly discussed.

LYNCH, St. Paul.

THE EFFECT OF VIVAX MALARIA ON SPINAL FLUID AND BLOOD SEROLOGIC TEST FOR SYPHILIS. HARRY M. ROBINSON JR. and WILLIAM W. MCKINNEY, J. A. M. A. **129**:544 (Oct. 20) 1945.

Serologic tests of the blood and examinations of the spinal fluid were made for 100 nonsyphilitic white men with malaria caused by plasmodium vivax. No change had occurred in the Kahn reaction of the spinal fluid of any of these patients. There were 33 per cent positive Kahn reactions of the blood and 11 per cent doubtful reactions. The serologic reaction for syphilis was negative in all cases at the end of eleven weeks.

DIAGNOSIS OF CHANCROID. ALBERT HEYMAN, PAUL B. BEESON and WALTER H. SHELDON, J. A. M. A. **129**:935 (Dec. 1) 1945.

Biopsy was performed in 59 of the 125 cases in this series, in which the patients were suspected of having either chancroid or venereal lymphogranuloma. A histologic diagnosis of chancroid was made in 45 cases. In 35 of these the diagnosis of chancroid was confirmed by cultures positive for Ducrey's bacillus.

On examination of the sections the lesion is found to consist of three zones. The surface zone, or base of the ulcer, is rather shallow and is made up of polymorphonuclear leukocytes, fibrin, red blood cells and necrotic tissue. Below this is a

fairly wide layer of edematous tissue, in which endothelial cells in various stages of proliferation outnumber all other cellular components. Newly formed blood vessels are numerous and may show palisading with occasional degeneration of the vessel walls and thrombosis. Finally there is a deep zone, which is densely infiltrated by plasma cells and lymphocytes.

Biopsy is limited to cases in which there are primary genital lesions; it is undesirable in patients with small lesions because of the pain involved. Cultural demonstration of the Ducrey bacillus can be accomplished in at least 75 per cent of all cases. Diagnosis by direct smears of material from the genital lesions is possible in approximately 50 per cent of the cases. Autoinoculation does not take with sufficient frequency to make it of value in routine work. The cutaneous test for chancroid is of limited value as an adjuvant to other procedures. In this group of 60 cases in which chancroid was the proved diagnosis positive reactions to cutaneous tests were found in only 46. A positive reaction persists for many years after an infection and therefore may not be significant in reference to the present illness.

Electroencephalographic Findings in Central Nervous System Syphilis: Before and After Treatment with Penicillin. J. Lamar Callaway, Hans Löwenbach, Ray O. Noojin, Beatrice H. Kuhn and Kathleen A. Riley, J. A. M. A. **129**:938 (Dec. 1) 1945.

No correlation exists between the degree of abnormality of the electroencephalographic pattern and the type, the severity or the duration of neurosyphilis. In the majority of cases a definitely but nonspecifically abnormal pattern or a pattern on the borderline between normal and abnormal is found. Thirty-eight patients suffering from neurosyphilis were studied before and after treatment with penicillin. Many whose former electroencephalograms showed abnormal patterns now have electroencephalograms in which the patterns are normal, and the records of most of the remaining ones show varying degrees of improvement. Abnormalities of the electroencephalographic patterns are interpreted as the expression of local cerebral anoxia and a generalized or localized cerebral inflammation.

Penicillin for Ulcers of Leg Treated by Pinch Grafts. Ruben Nomland and Evelyn G. Wallace, J. A. M. A. **130**:563 (March 2) 1946.

A series of 9 cases is reported in which ulcers of the leg were treated by the application of pinch grafts and in which penicillin was used before and after the grafting to control the surface infection caused by beta hemolytic streptococci and hemolytic Staphylococcus aureus. These infections are the chief cause of failure of the skin grafts to take. It is recommended that penicillin be injected intramuscularly before and after grafting of skin in all cases in which ulcer of the leg is treated by pinch grafts.

Treatment of Early Syphilis with Penicillin. Arthur G. Schoch and Lee J. Alexander, J. A. M. A. **130**:696 (March 16) 1946.

Penicillin properly administered will cure the majority of patients with primary and secondary syphilis. The use of 2,400,000 units of penicillin in seven and a half days (40,000 units intramuscularly every three hours) is advocated. In addition, five intramuscular injections of 0.2 Gm. of bismuth salicylate are given at two day intervals. Intimate contacts of the patients should be treated coincidentally to avoid reinfection.

Henschel, Denver.

Testosterone Propionate in Treatment of Senile Pruritus. W. L. Dobes, Jack Jones and Andrew G. Franks, J. Clin. Endocrinol. **5**:412 (Dec.) 1945.

Dobes, Jones and Franks briefly review the literature on the effects of androgens used in the treatment of various dermatoses. After discussing the difficulties in making an accurate diagnosis of "senile" pruritus, they report the results of treat-

ment with testosterone propionate and methyl testosterone—the former administered topically and by injection and the latter given orally. The oral use of methyl testosterone was found to be completely ineffectual. Testosterone propionate by inunction was fairly successful in controlling the pruritus but yielded the best result when given subcutaneously.

Both symptoms and visible changes were relieved in 7 patients, and diminished in 2; in 1 there was no relief.

LYNCH, St. Paul.

SPECIFICITY OF STREPTOCOCCI ISOLATED FROM PATIENTS WITH SKIN DISEASES: STUDIES ON PEMPHIGUS, DERMATITIS HERPETIFORMIS, LUPUS ERYTHEMATOSUS AND ERYTHEMA MULTIFORME. ASHTON L. WELSH, J. Invest. Dermat. **7**:7 (Feb.) 1946.

The morphologic, cultural, staining and fermentation characteristics of streptococci which were isolated from patients who had pemphigus are described. The streptococci were shown to have a characteristic cataphoretic mobility distribution curve and were found to be virulent for five species of animals. They also produced lesions consistent with those of pemphigus in a few instances.

The different strains of organisms were shown to be serologically identical by: (1) agglutination reactions between the various strains and serums of a horse and rabbits which had been immunized against organisms isolated from the patients; (2) reciprocal agglutinin absorption; (3) precipitin reactions between the aforementioned immune serums and alkaline saline extracts of the streptococci isolated from the patients; (4) precipitin reactions between the immune serums and the specific soluble polysaccharide substances; (5) the cataphoretic mobility-reducing action of immune serums, and (6) the reciprocal absorption of the immune serums so that these no longer showed the specific mobility-reducing action.

A specific relationship between the patients who had pemphigus and the streptococci was demonstrated by (1) precipitin reactions between the nasopharyngeal washings and the serums of animals immunized with the specific organisms; (2) precipitin reactions between the blister fluid and the serums of the immunized animals; (3) precipitin reactions between alkaline saline extracts of the organisms and the serums of patients who had pemphigus; (4) precipitin reactions between the specific soluble polysaccharide substances and the serums of these patients; (5) the cataphoretic mobility-reducing action of the patients' serums on the organism; (6) absorption of the antibodies of their serums by heterologous strains of the streptococci so that these serums no longer showed this specific mobility-reducing action; (7) production of bullae in the patients by intradermal and subcutaneous injection of dead organisms and (8) production of the erythema-edema (EE) reaction of Foshay by intradermal injection of immune horse serum.

It was also shown that streptococci isolated from patients who had dermatitis herpetiformis, disseminated lupus erythematosus and erythema multiforme exudativum, respectively, were similar to, but not identical with, the streptococci isolated from patients who had pemphigus.

A NEW TREATMENT FOR ANTHROPOPHILIC TINEA TONSURANS (MICROSPORON AUDOUINI). GEORGE MILLER MACKEE, FRANZ HERMANN and FLORENTINE L. KARP, J. Invest. Dermat. **7**:43 (Feb.) 1946.

Based on the results of histologic, mycologic and biochemical experiments, studies were made on the therapeutic effect of trimethyl cetyl ammonium pentachlorphenate in a proprietary vehicle. This fungicide solution was used in combination with an acid-buffered detergent. The treatment resulted in a cure in 54 per cent of the treated patients in approximately fourteen weeks.

This new form of therapy presents a major handicap in the technic of application, and therefore the authors suggest that its use is particularly indicated in those cases in which roentgen ray epilation is not possible or has failed.

EVALUATION OF MEASURES FOR USE AGAINST COMMON FUNGOUS INFECTIONS OF SKIN. M. B. SULZBERGER, C. SHAW and A. KANOF, U. S. Nav. M. Bull. **45**:237 (Aug.) 1945.

The object of this study was to test the comparative values, for the prophylaxis and the treatment of fungous infections of the feet and the groins, of the following materials: (1) undecylenic acid–zinc undecylenate powder, (2) sodium propionate powder, (3) boric acid–salicylic acid powder, (4) undecylenic acid–zinc undecylenate ointment and (5) clothing impregnated with Impregnite CC3 by the water-in-oil emulsion process.

The results in prophylaxis revealed that active fungous infections developed in the feet of: (1) 8.85 per cent of the men using no prophylactic measures; (2) 8.33 per cent of the men who wore an impregnated sock; (3) 11.15 per cent of the men using boric acid–salicylic acid powder; (4) 3.10 per cent of the men using sodium propionate powder, and (5) 1.07 per cent of the men using undecylenic acid–undecylenate powder.

The results in the treatment of active and usually bilateral fungous infections of the feet indicated that: (1) Impregnated socks were of no value; (2) propionate powder and undecylenate powder were equally effective, and (3) undecylenic acid–undecylenate powder and undecylenic acid–undecylenate ointment were also equally effective.

In the treatment of active fungous infections of the groin, the results were as follows: (1) Undecylenic acid–undecylenate powder effected cures in 35 cases and improvement in 8 and was of no effect in 1; (2) sodium propionate powder effected cures in 10 cases and improvement in 3 and was of no effect in 4, and (3) impregnated clothing made the infections in 4 cases worse and was of no effect in 7.

RODIN, South Bend, Ind.

ARSENICAL ENCEPHALOPATHY. G. A. RANSOME, J. C. S. PATERSON and L. M. GUPTA, Brit. M. J. **1**:659 (May 12) 1945.

Five patients with arsenical encephalopathy were successfully treated by a program which emphasizes the value of the sitting posture for these patients.

"Decongestion" can be achieved simply by the patient's sitting up against a back rest. Lumbar puncture and dehydration of the brain with concentrated serum albumin or hypertonic dextrose solution were also employed.

PENICILLIN CREAM OF LOW CONCENTRATION. G. H. DU BOULAY, Brit. M. J. **1**:50 (Jan. 12) 1946.

Thirty-nine patients with staphylococcic and streptococcic infections of the skin were treated with a penicillin cream containing 200 units of penicillin per cubic centimeter. The cream also contained 2 cc. of 2-phenoxy-ethanol.

The author concludes that if impetigo has been present for five weeks or less it will heal in from three days to two weeks provided treatment is continued until no mark remains on the skin. Chronic impetigo and sycosis barbae fail to clear with this cream. No evidence of a sensitive strain becoming resistant during treatment was found.

DERMATITIS DUE TO SULPHAGUANIDINE. BASIL HAIGH, Brit. M. J. **1**:52 (Jan. 12) 1946.

A patient with a probable solar dermatitis, who had an ulcer of the leg, was treated with sulfanilamide powder locally, without success. Six weeks later he was given sulfathiazole by mouth, following which a papular eruption developed on the legs and the trunk. Two months later he was admitted to the hospital with bacillary dysentery, for which he was given sulfaguanidine. Two days later he presented an eruption identical with that of the previous sulfathiazole dermatitis, which was limited to the sunburned areas of the skin. The results of patch tests with sulfanilamide and sulfaguanidine on nonsunburned areas were negative.

SHAW, Chattanooga, Tenn.

Society Transactions

MINNESOTA DERMATOLOGICAL SOCIETY

S. E. Sweitzer, M.D., *President*

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Feb. 9, 1945

Chronic Lupus Erythematosus of the Face and the Tongue. Presented by Dr. S. E. Sweitzer, Minneapolis.

E. R., a white woman aged 52, first began to have a cutaneous disease in the summer of 1943. The first attack affected both elbows and then the arms and the legs. The entire face and the ears were involved with a red, swollen eruption which included blisters. In the fall of 1943 the eruption subsided, only to recur in the summer of 1944. This second attack involved the same areas as the first, but in the fall it persisted in patches over the nose, the malar region and the lips, behind the ears and on the forearms and the lower portions of the legs. Her health was good until 1933, at which time she contracted amebic dysentery in Chicago. A hysterectomy for fibroids was done that year.

The leukocyte count was 6,600; the differential and the erythrocyte count were normal, as was the urine. The serologic tests for syphilis gave negative results. The tuberculin reaction was strongly positive.

An examination revealed dull red patches, several centimeters in diameter, across the bridge of the nose and on both cheeks. There was also a patch on the dorsum of the left hand and behind the left ear. The plaques were dry and had small adherent scales. On the left side of the tongue near the posterolateral margin was an ill defined irregular plaque.

Histologic sections of the tongue and the cutaneous lesions were shown.

DISCUSSION

Dr. J. F. Madden, St. Paul: I think that it is common to have transitory benign plaques like these associated with scrotal tongue. I do not think that the lesions on the tongue are those of lupus erythematosus.

Dr. L. H. Winer, Minneapolis: Microscopically, there are follicular dilatation, plugging of the follicles by nucleated cells instead of non-nucleated cells and lymphocytic infiltration. Also favoring the diagnosis of lupus erythematosus is the atrophy of the mucous membrane. One does not see atrophy in transitory benign plaques of the tongue.

Dr. S. E. Sweitzer, Minneapolis: I still think that it is a benign transitory plaque.

Pemphigus Vulgaris of the Mucous Membrane. Presented by Dr. H. E. Michelson, Minneapolis.

Mrs. H. M., a white woman aged 56, was first seen at the University Hospitals, Minneapolis, in September 1944, with an eruption in the mouth of about ten years' duration, especially severe for the past three years. No definite bullae were observed on any other part of the body except the mucous membrane of the mouth. Previous medicament consisted of germanin, acetarsone, oxophenarsine hydrochloride, tryparsamide, Asiatic pills (a preparation of arsenic trioxide and black pepper) and sulfapyridine. The patient had a severe reaction from germanin and no improvement from any of the medicaments. Treatment at the University Hos-

pitals consisted of a series of vaccinations with smallpox vaccine. The patient reacted strongly to the first vaccination and remained immune thereafter. No improvement was noted in the lesions of the mucous membrane.

Serologic tests for syphilis were negative. On December 18, 5 mice were inoculated intracerebrally with fluid from the blisters of the roof of the mouth. The animals were observed for five weeks and showed no signs of illness.

An examination showed bullae on the hard palate, the buccal mucosa and the inner surfaces of the lips. Erosions of the sites of ruptured bullae are present.

DISCUSSION

There was no discussion of this case.

Lichen Planus of the Mucous Membrane and the Eyelid. Presented by Dr. L. H. Winer, Minneapolis.

Mrs. A. A., a white woman aged 40, stated that an eruption broke out in her mouth in July 1944. About a month later a lesion formed on the right lower eyelid. She had been treated by a physician and a dentist for Vincent's infection of the mouth. In the past two weeks the gums had become eroded and tender at the border of the teeth. In the past eight weeks she received 1 cc. of 10 per cent bismuth subsalicylate in oil once a week intramuscularly.

On examination the buccal mucosa of each cheek showed whitish papules, arranged in rings and striations. The right lower eyelid had a plaque measuring 1 by 1 cm. The border of this red plaque consisted of discrete angulated small papules.

The histologic examination of a biopsy specimen from a papule of the right wrist showed the epidermis hyperkeratotic and the epidermal cells undergoing eosinophilic degeneration. There were the typical vesicular degeneration of the basal cells and formation of Joseph's spaces in the epidermis-cutis border. There was a dense round cell infiltration in the upper part of the cutis which closely approximated the epidermis and had a sharp lower border. This lower border extended to the reticular layer of the cutis, which itself was otherwise uninvolved.

DISCUSSION

There was no discussion of this case.

Nevus Unius Lateris. Presented by Dr. S. E. Sweitzer, Minneapolis.

W. D., an Indian woman aged 20, was admitted to the Minneapolis General Hospital for delivery of her first child on Jan. 30, 1945. She stated that a birthmark had always been present on her left cheek and over her left ear but that during the past year it almost doubled its size.

An examination revealed a brownish gray irregular tumor, the size, the shape and the thickness of a man's thumb, extending down over the left cheek. The tumor became smaller as it curved over the left ear and gradually disappeared behind the ear. The mass was somewhat tender, and pressure expressed a thick whitish material from crevices which gave a lobulated appearance to the tumor. The rest of the skin was normal save for a coffee-colored spot, measuring 3 by 2 cm., on the internal surface of the left arm.

Histologic sections were shown.

DISCUSSION

There was no discussion of this case.

Lingua Nigra. Presented by Dr. S. E. Sweitzer, Minneapolis.

M. K., a white woman aged 27, stated that her tongue first became black eight months ago and that it remained so for two months. There have been several recurrences since, lasting for a few days. Three weeks ago it again became

black. She stated that on the basis of a papular eruption a diagnosis of syphilis was made in September 1944 and she was given eleven intramuscular injections. In November she entered the Minneapolis Treatment Center and was given 1,200,000 units of penicillin over a period of eight days.

An examination revealed a brownish black coating covering the posterior two thirds of the tongue on its dorsal surface. The papillae are slightly hypertrophic, but no long, hairlike lesions were seen.

DISCUSSION

There was no discussion of this case.

Abortive von Recklinghausen's Disease. Presented by DR. S. E. SWEITZER, Minneapolis.

C. P., a white woman aged 66, has had lesions on her right forearm since she was 21 years of age. Small nodules developed on the right forearm, increased to their present size rather quickly and have remained stationary ever since. The patient's general health had always been good except that in 1930 the uterus was removed because of fibroids. There was no history of any cutaneous tumors in any members of her family. Roentgenograms showed that the long bones were normal.

An examination revealed twenty to thirty small nodules, varying in size from that of a pinhead to that of a pea. The only area involved is the anterior surface of the right forearm. The nodules are flesh colored and soft and are not painful. There are several scars due to the removal of the lesions by cautery. The rest of the body is clear. There is no hyperpigmentation.

Microscopic sections were shown.

DISCUSSION

DR. L. H. WINER, Minneapolis: About six weeks ago I had occasion to use radon ointment on ulcers of the leg and had some left over. On that day a patient with granuloma annulare came in, and I put some of the radon ointment (200 electrostatic skin units per cubic centimeter) on three of the lesions. The following week I put radon ointment (200 electrostatic skin units per cubic centimeter) on again for twenty-four hours. I saw the patient yesterday, and the lesions have disappeared, leaving only brown spots.

DR. S. E. SWEITZER, Minneapolis: What is in the solution?

DR. L. H. WINER, Minneapolis: Radium emanation in petrolatum. It loses 7 per cent of its strength each day.

DR. S. E. SWEITZER, Minneapolis: The emanation is gone in practically four days.

A Case for Diagnosis (Pityriasis Rubra Pilaris in One of Twin Brothers?). Presented by DR. L. H. WINER, Minneapolis.

S. I., a boy aged 14, complains of painful fissures and thickening of the skin of the palms and the soles for the past year. This condition was aggravated during the cold weather of the winter months and improved during the summer. He also gave a history of having had hay fever, for which he has been treated.

The skin on his palms is thickened and fissured, as is the skin on his soles. The dorsal aspect of the fingers shows thickening and redness of the skin over the knuckles. There is also a plaque of dermatitis on his left elbow. Granular lesions about 1 mm. in diameter can be seen on the mucous membrane of the anterior tonsillar fold just above the level of the lower molar teeth.

DISCUSSION

DR. PAUL O'LEARY, Rochester, Minn.: The lesions have the earmarks of a neurodermatitis rather than those of pityriasis rubra pilaris. The plaque on the left elbow of comparatively recent origin is of the type of lichen chronicus simplex.

DR. L. H. WINER, Minneapolis: Dr. Sweitzer also saw this patient, and he thought that there probably was a vitamin A deficiency. He has been given 100,000 units of vitamin A for a period of two months. However, I feel the same as Dr. Sweitzer, that this is a keratosis on the basis of a vitamin A deficiency.

Pityriasis Lichenoides et Varioliformis Acuta. Presented by DR. S. E. SWEITZER, Minneapolis.

D. B., a boy aged 6 years, first noticed small red lesions on the right forearm near the shoulder one year ago. A few more lesions developed, and then the patient contracted measles. Following this, additional scaling, crusting and papular lesions developed over the entire body. These lesions have disappeared and reappeared since that time, and many have healed, leaving a fine atrophic scar. There was no itching or other symptom, and his general health was always good.

An examination revealed scattered erythematous papules with scaling and crusting over the face, the trunk and the extremities. They are 3 to 5 mm. in diameter; some show a thick crust, and others show a thin silvered scale. Many scars point out the location of previous lesions.

The histologic examination of a recent (young) lesion showed a parakeratotic scale which lay on a fairly normal epidermis. The basal cells of the epidermis in this involved area were difficult to differentiate from the cells of the cutis in that the epidermis took a more intense eosinophilic stain. There were faint suggestions of vesicle formation in the epidermis underneath the parakeratotic scales. The cutis contained a moderately heavy perivascular round cell infiltration. The connective tissue stained deeply with eosin, and the lymphatic spaces were intensely dilated.

Rosacea of the Nose: Tuberculoid Structure in Histologic Section. Presented by DR. L. H. WINER, Minneapolis.

Mrs. G. C., a white woman aged 62, has had an eruption on the nose for the past ten years. Three years ago, after roentgen ray treatment, it disappeared, but during the present winter it has recurred.

On examination the skin on the tip of the nose was thick and boggy and showed numerous small nodules, 1 to 2 mm. in size, which were red and were completely expressed on diascopy. A test with old tuberculin (1:1,000) elicited a negative reaction. Treatment consisted of applications of peeling pastes, which produced an improvement.

Histologic sections were shown.

DISCUSSION

DR. S. E. SWEITZER, Minneapolis: I thought that this case ought to be presented because some cases have been presented as rosacea-like tuberculid of Lewandowski and many are not really cases of tuberculosis.

DR. FRANCIS LYNCH, St. Paul: Are the microscopic changes truly tuberculoid or only those of chronic granulomatous inflammation? It is not a typical tuberculoid structure.

DR. L. H. WINER, Minneapolis: I do not know of any other way of putting the point across.

DR. FRANCIS LYNCH, St. Paul: It is not a typical tuberculoid structure.

DR. L. H. WINER, Minneapolis: Tuberculoid, yes, but not tuberculous.

Pyoderma Faciale. Presented by DR. S. E. SWEITZER, Minneapolis.

A. H., a white woman aged 23, first had an eruption on the face in 1938 during her first pregnancy. This eruption subsided two months after delivery. In 1941 it recurred at the sixth month of the second pregnancy, and she was seen in the

outpatient department of the Minneapolis General Hospital, at which time a diagnosis of rosacea was made. This attack lasted for two years, after which her skin was completely clear. There were no deep pustular elements or tendency toward scar formation at that time. The third recurrence began in October of 1943, at the beginning of the third pregnancy, and became progressively worse. After delivery a large amount of pus drained from the sinuses, and boggy hypertrophic nodules appeared. She was seen in the outpatient department of Minneapolis General Hospital in September of 1944, at which time pustular and keloidal elements involved the forehead, the face and the submental area. The rest of the body remained completely free. There was no previous history of cutaneous disease. The general health has always been good. Serologic tests for syphilis were negative. The results of hematologic and urinary studies were within normal limits. In treatment 1,500,000 units of penicillin was administered between September 30 and November 8. After the administration of penicillin the pustular discharge improved greatly, and between Nov. 21, 1944, and this date she has received eight roentgen ray treatments (88 r each) at weekly intervals.

An examination revealed bluish red nodules and linear hypertrophic scars on the forehead, the face and the submental areas. There is no suppuration at the present time.

DISCUSSION

Dr. Paul O'Leary, Rochester, Minn.: This woman looked considerably older than 23. The history I obtained is identical with that of many of the girls who have pyoderma faciale. Since her last pregnancy she has gained 40 or more pounds (18 or more kilograms) and has had amenorrhea. The pyoderma, obesity and amenorrhea appeared simultaneously. I have been repeatedly impressed with the frequency of menstrual dysfunction and this eruption, so much so that my therapeutic efforts are directed mainly toward reestablishing a normal menstrual cycle. Cultures from the burrowing tracts are usually sterile; hence antiseptics taken locally or by mouth are directed only to the secondary infection that occurs in these lesions after they are manipulated. The gynecologists should determine the type of ovarian dysfunction she has and direct their efforts to correcting it.

The significance of the part glandular dysfunction plays in this disease is noted especially in the unmarried young women with pyoderma faciale who are underweight, flat chested, anemic and amenorrheic. Not only does the eruption abate with the proper glandular therapy, but also there is a striking improvement in the patient as noted by gain in weight, enlargement of the breasts, return of menses and other physical changes. All the dysfunctions noted in these young women are not of the same type; hence it is not possible to give them all the same glandular therapy. Consequently each case must be evaluated individually.

Roentgen ray therapy has also helped some of my patients, especially those in whom the ovarian dysfunction was not clearcut.

Dr. C. D. Freeman, St. Paul: I gave the patient penicillin, without any results. With sulfathiazole I got excellent results.

Dr. Paul O'Leary, Rochester, Minn.: It has been my experience in culturing material from the sinus tract that the cultures have been essentially sterile.

Dr. J. F. Madden, St. Paul: I have been giving sulfathiazole by mouth combined with the usual treatment for acne associated with large abscesses and have obtained much better results than I ever have with any other treatment.

Bullous Lichen Planus. Presented by Dr. S. E. Sweitzer, Minneapolis.

M. DeF., a white woman aged 29, was presented on Sept. 15, 1944 at the meeting of the Minnesota Dermatological Society as having bullous lichen planus. At that time large bullae were present on the arms and the legs, with a few lesions on the abdomen. Typical papules of lichen planus were also present. Shortly afterward the eruption became generalized and involved the entire body, including the face. The patient was hospitalized, and wet compresses were used. Sodium salicylate and sulfadiazine were each tried with no effect, and on Oct. 12,

1944 treatment with acetarsone was begun according to the Oppenheim technic. There was decided improvement during the first week, and the treatment was continued until Jan. 15, 1945.

An examination as of this date showed only pigmented scars, mostly on the lower extremities but with a few on the arms, the abdomen and the back.

DISCUSSION

There was no discussion of this case.

Atrophoderma Hypoestrogenicum. Presented by Dr. S. E. Sweitzer and Dr. L. H. Winer, Minneapolis.

M. T., a white woman aged 30, has had a plaque type of eruption since she was 11 years old. It first began as a small reddish area on the anterior surface of her ankle and spread to involve both extremities. In the Archives of Dermatology and Syphilology (**24**:842 [Nov.] 1931) she was presented by one of us (S. E. S.) as having *tuberculide en plaque.* At puberty there was about one year of freedom from the eruption, but it recurred in the form of 1 to 5 cm. oval or round or gyrate plaques elevated above the surface of the skin. There was a tendency for the lesions to group, and they were never scaly. The color was dusky red, and the atrophic scars of previous lesions were visible. The extremities were the only sites of the eruption. She had borne two children, one in 1939 and the second in 1943. During the fourth month of each pregnancy, the eruption completely cleared only to reappear the fourth or the fifth month post partum. A diagnosis of latent syphilis was made in 1934 on the basis of positive serologic tests. Between 1934 and 1937 she received routine antisyphilitic treatment. Tuberculin reactions have always been negative. Serologic tests for syphilis have been negative since 1936. Leukocytes numbered 7,000 on Dec. 1, 1944, and 10,150 on December 23. The differential count showed 5 per cent lymphocytes on December 23. The blood cholesterol level was 150 mg. per hundred cubic centimeters in October 1944. On several occasions roentgenograms showed that the chest and the long bones were normal. On October 12 diethylstilbestrol was given, and the dose was increased so that after one week she was taking 1.5 mg. daily. This was continued until November 2 when it was discontinued until December 5. Since then she has been taking 3 mg. daily for two weeks out of every month, with little effect on normal menstruation. Two months after diethylstilbestrol therapy was started there was a spectacular abatement in the eruption, the lesions having faded and flattened.

An examination revealed a few lightly pigmented areas, 2 or 3 cm. in diameter, on the upper extremities, which were the remains of previous plaques. A few slightly raised purplish plaques, 2 to 4 cm. in diameter, remained on the lower extremity at the site of the previous eruption.

Histologic sections were shown.

DISCUSSION

Dr. S. E. Sweitzer, Minneapolis: Dr. Winer has been taking care of the patient for years. Her eruption comes and goes.

Dr. Stephen Rothman, Chicago: I should like to ask whether or not the patient has hyperthyroidism. She displays a slight degree of exophthalmos.

Dr. L. H. Winer, Minneapolis: Her basal metabolic rate was normal. Also her blood cholesterol level was 150 mg. per hundred cubic centimeters.

Dr. H. E. Michelson, Minneapolis: How do you correlate all the findings in this patient 19 years of age? Why the giant cells? Is there any relationship between the theelin and the findings?

Dr. L. H. Winer, Minneapolis: In view of the history of these lesions occurring and disappearing with pregnancy and recurring after pregnancy, this patient was shown to Dr. John McKelvey. He advised giving her diethylstilbestrol, 5 mg., three times a day. Two biopsies were made of two of the active lesions.

From a microscopic section and on staining a frozen section for fats, it was found that there was an excessive amount of fat in the infiltrated zone. The pathologist could give no help on any differential stains to show specificity of the fat. The reason I mention fat is that the fat could account for the formation of giant cells, because capsule lipids of the tubercle bacillus have been known to cause formation of giant cells. After the inflammation receded, the microscopic section showed a reduced cellular infiltration and also a reduction in the amount of fat in the tissue. The elastic tissue in these areas was gone. Because the elastic tissue has disappeared and the skin shows atrophy clinically, we decided to call it atrophy. We call it hypoestrogenic because the resorption occurred with the administration of stilbestrol. We are still doubtful of this patient's maintenance dose of stilbestrol. We stopped giving her stilbestrol two weeks ago, after she had taken 1 mg. three times a day for two weeks. She started to menstruate six days ago and is still menstruating. It is unusual for her to menstruate so much. Dr. John McKelvey suggested that we reduce the dose of stilbestrol to 3 mg. per day because he thought that we might get hypertrophy of the endometrium which might necessitate the removal of the uterus. With that idea in mind, we have made platelet counts, which were within normal limits, 300,000 per cubic millimeter.

Dr. Carl Laymon, Minneapolis: In my opinion the term "atrophoderma hypoestrogenicum" does not fit this case. There is no atrophy, and except for the history of improvement during pregnancy there is nothing which even pertains to ovarian function. The patient has no signs of a lack of estrogens and has had two normal pregnancies. The lesions clinically fit better a diagnosis of sarcoid, and even the histologic data can be fitted in with such a diagnosis.

Dr. S. E. Sweitzer, Minneapolis: I suggest that if she is having trouble menstruating she had better stop the stilbestrol. It only seems to alleviate the condition.

Dr. Francis Lynch, St. Paul: The disappearance of her eruption at puberty throws considerable doubt on the thought that the eruption results from estrogenic deficiency. Perhaps some other endocrine disturbance is responsible.

Dr. S. E. Sweitzer, Minneapolis: I think that either sarcoid or tuberculosis is the proper diagnosis in this case. I was never much inclined to this hypoestrogenic diagnosis in her case, but Dr. Winer wanted to see what he could do with the eruption; so I let him.

Dermatitis Medicamentosa. Presented by Dr. S. E. Sweitzer, Minneapolis.

L. H., a white woman aged 34, was taking phenobarbital, ½ grain (30 mg.) three times a day, because of high blood pressure. She also was taking a capsule containing sodium iodide, phenobarbital and theobromine. The use of both these drugs was begun two weeks before the onset of the eruption. An ovarian cyst was removed in March 1944, and a gynecologic operation was performed in 1930. Three weeks ago she was seen in the Minneapolis General Hospital with a general scarlatiniform eruption. It also involved the conjunctivas, the lips, the entire mouth and the throat, which were intensely red and dry; the mucous membrane resembled that of previous patients with eruption due to phenobarbital. On the legs and the lower part of the abdomen the eruptions were morbiliform. The temperature of the patient on admission to the hospital was 105 F. The leukocyte count was 3,800, of which 92 per cent were lymphocytes. There was a gradual fading of the color of the eruption.

An examination revealed a dull red skin, especially pronounced on the face. There was slight scaling of the face and the backs of the hands. The mucous membranes were still dry and injected.

DISCUSSION

Dr. S. E. Sweitzer, Minneapolis: I recall the deaths of 3 patients who had dry red skins, dry red mouths and tongues and high temperatures. This girl took extremely small doses of phenobarbital and had a high temperature.

Keratosis Blennorrhagica. Presented by Dr. S. E. Sweitzer, Minneapolis.

R. D., a white man aged 23, first noticed a urethral discharge five weeks ago. For three weeks he did nothing about it, and on Jan. 23, 1945 he was admitted to the Minneapolis General Hospital with acute gonorrheal urethritis and acute arthritis involving the left ankle, knee and wrist and the little finger of the left hand. His temperature ranged between 100 and 102 F., and he had a leukocyte count of 13,400. Urethral smears have been positive for gonococci. On January 23 he began to take sulfadiazine, 1 Gm. every four hours, and on January 25, because his condition was becoming worse, he was given 300,000 units of penicillin over the next four days. The lesions on the feet have been present for two weeks.

An examination revealed diffuse thickening on the plantar surfaces of both feet. Irregularly arranged over this area were hornlike projections from split pea to hazelnut size. On the dorsum of the left hand and wrist and on the left knee and ankle are numerous large vesicles and crusts. These areas have been subjected to hot packs.

DISCUSSION

Dr. Paul O'Leary, Rochester, Minn.: Some of the members are no doubt familiar with the syndrome recently described by Dr. Reiter, in which there is a urethral discharge in which gonococci are not demonstrable, associated with conjunctivitis, arthritis and a bizarre type of dermatitis. Several of my former associates have seen soldiers who returned from overseas with the syndrome. The small amount of penicillin which was given this patient at long intervals might account for the lack of improvement, and it would seem advisable to try it again, with at least 1,000,000 units being given in a period of three days. The smears from the urethral discharge were positive for gonococci, but as I understand the matter they became negative before the penicillin was given.

Keratosis blennorrhagica is an extremely rare disease in my experience, and accordingly the clinical picture is far from clear in my mind. Patients with chronic infectious arthritis of nongonorrheal origin will occasionally display inspissated and hyperkeratotic lesions, especially if the nursing care has been neglected. The study of Reiter's syndrome and gonorrheal keratosis blennorrhagica should be combined with the hope of eliciting some additional information about both diseases.

Dr. Stephen Rothman, Chicago: I saw 2 cases of keratosis blennorrhagica. In both cases gonococcic septicemia was present, and both patients had arthritis and endocarditis. In the beginning both neglected their gonorrhea, and each went to see a physician after he had had severe prostatitis for several weeks. Diffuse keratoses, but no papular elements as in the presented case, were present on the soles, the palms and the elbows. Both patients died, because this happened long before the era of modern chemotherapy. I should like to ask whether penicillin has been used in gonococcic endocarditis and septicemia and with what result.

Dr. Paul O'Leary, Rochester, Minn.: I have had no experience, although reports are indicated.

Dr. Stephen Rothman, Chicago: I hear that in the presented case the keratosis did not respond to penicillin.

Dr. Paul O'Leary, Rochester, Minn.: It might be the small dose and that there was a lapse of time. It might be that a million units would make a different picture.

Squamous Cell Epithelioma of Sebaceous Gland Origin. Presented by Dr. S. E. Sweitzer, Minneapolis.

M. H., a white man aged 77, has had a tumor on the back of his neck for three years. At times it broke open and ulcerated. Twenty-five years ago a cancer was removed from the right cheek with radium. In 1937 roentgen rays were successfully applied to an epithelioma on the right side of the nose, and in 1939 cautery was used on a lesion of the right temple.

An examination revealed the scars of the three previous lesions. On the back of the neck was a button-like tumor, 2 cm. in diameter. The tumor was red and had a slight central depression. It was entirely above the surface of the skin and freely movable.

The histologic examination showed the epidermis to be present in some areas and absent in others and the tissue to be ulcerated. Lying beneath the epidermis and in the ulcerated area were nests of cells well walled off, the contour of which assumed that of sebaceous glands, and these cells in the basal zones appeared foamy as do sebaceous cells. In other zones higher up or more toward the center of the proliferating mass, these cells had become keratinized, and the nuclei had become darker and contained mitotic figures.

DISCUSSION

DR. STEPHAN EPSTEIN, Marshfield, Wis.: This is a somewhat odd tumor. Clinically it looks like a basal cell epithelioma, being made of a rather soft grayish translucent tissue. The location at the back of the neck is somewhat unusual.

Microscopically it is an atypical tumor composed mostly of cells with dark-staining nuclei, many of them spindle shaped, presenting the appearance of basal cells. There are a few spots where an attempt at pearl formation is made. However, these are not real horn pearls but what Darier called parakeratotic pearls. This picture would fit in well with that type of epithelioma that is called by Darier *epithelioma metatypique mixte.*

DR. L. H. WINER, Minneapolis: Dr. Hamilton Montgomery calls these cells "cells with individual cell keratinization." Ordinarily the sebaceous cell is a basal cell which secretes, but when a basal cell forms keratin and shows mitoses, as some of these cells do, then it is called a squamous cell epithelioma.

Macular Atrophy. Presented by DR. S. E. SWEITZER, Minneapolis.

L. H., a white woman aged 70, has had generalized itching of the skin for the past six months. She was not aware of the presence of white spots.

An examination disclosed irregular whitish spots with wrinkled, atrophic skin. The lesions were grouped and extended along the upper part of the chest over the clavicle and on to the side of the neck. One or two of the areas showed follicular plugging.

The histologic examination revealed hyperkeratosis and also epidermal atrophy in the sense that the papillary bodies had disappeared. The sebaceous glands were absent, but the sweat glands were present. The upper portion of the cutis showed zones of homogenization, under which there were bands of round cell infiltration.

DISCUSSION

DR. STEPHEN ROTHMAN, Chicago: This woman is suffering from an inflammatory eruption. She states that she has had generalized itching for the past six months, and now diffuse reddening and scaling can be seen. There are a few atrophic scars in the inflamed areas, but I do not see any sign of idiopathic atrophy. The histologic section does not substantiate this diagnosis either. It is true that macular atrophy, or anetoderma of Jadassohn, is described as starting with mild inflammation, but this is of short duration. It is my feeling that the initial inflammatory phase has been overemphasized in the literature. The essential primary change in macular atrophy is atrophy of the elastic fibers.

DR. PAUL O'LEARY, Rochester, Minn.: The atrophic plaques on the left side of the neck had definite plugs which suggested the diagnosis of lichen sclerosus et atrophicus.

DR. FRANCIS LYNCH, St. Paul: On the chest, especially under the breast, one can see shiny flat papules, of pinhead size, fairly characteristic of lichen sclerosus et atrophicus. The sections do not confirm that diagnosis, but the tissue was removed from a site where a complicating dermatitis is present.

Keratosis Follicularis. Presented by DR. S. E. SWEITZER, Minneapolis.

J. S., a white man aged 74, was presented at the meeting of the Minnesota Dermatological Society on April 14, 1939. The eruption has been present as long as he can remember, and in recent years he has had no treatment. The eruption has progressed and is more extensive than it was in 1939. In January of 1945 his left leg was removed because of arteriosclerotic gangrene.

A moist eruption is seen in the groins and axillas and on the sides of the neck. It is covered with a greasy scale, and is foul smelling. Toward the periphery of the moist plaques the eruption becomes distinctly papular with crusted lesions, 3 to 5 mm., which are present also on the lower part of the abdomen and on the back.

The histologic examination of the thinner of the two biopsy specimens revealed hyperkeratosis with extreme formation of lacunas in the epidermis. A few *corps ronds* were seen in the region of the epidermis which formed the floor of the lacunas. Grain cells were not in evidence in this section.

DISCUSSION

There was no discussion of this case.

Mycosis Fungoides. Presented by DR. S. E. SWEITZER, Minneapolis:

A. A., a white woman aged 72, has had an eruption for the past ten years. At no time was the skin completely clear, but there has been one episode after another of exacerbation and remission, with the exacerbations becoming more severe and prolonged in recent years. She was admitted to the Minneapolis General Hospital fifteen times during the past five years. The eruption was confined mainly to the following sites: face, ears, scalp, neck, axillas, submammary regions, umbilicus, groin, popliteal spaces and the lower portions of the legs. There has always been much edema with exudation and fissuring to form ill defined plaques, on which later moderately thick but loosely adherent white scales develop. Greases have been poorly tolerated, and roentgen rays in fractional doses did not help. The involved areas have responded best to wet packs and lotions. Itching has never been a prominent feature, but excoriations have often been present.

From 1940 to 1942 the leukocyte count ranged from 5,000 to 7,000, with a normal differential count, but since 1943 there has been leukopenia (from 1,800 to 4,000 cells) 40 to 60 per cent of the cells being lymphocytes. In June 1944 a biopsy of sternal bone marrow was performed, and numerous reticulocytes were seen which were thought to be of a low grade malignancy. Cutaneous imprints, taken in June and subsequently stained with Wright's stain show the same immature reticulum cells to be present in the skin.

Serologic tests for syphilis were negative. Other laboratory procedures revealed no abnormalities with the exception of occasional albumin in the urine. A tuberculin test elicited a positive reaction. The previous health of the patient was good except for a drainage of the gallbladder in 1924 and a vein-stripping operation for varicosities of the lower extremities years ago. There have been occasional spells of vertigo and weakness, and one month ago the patient had an attack of cystitis.

An examination revealed an ill defined scaly eruption on the face, the ears and the abdomen, beneath the breasts, in the groins and on the lower extremities. In the groins, the axillas and the popliteal spaces and behind the left ear there is a tendency toward fissuring and exudation. The scalp is thickly covered with a gray adherent scale. When the scale is removed from the lesions of the glabrous skin, a bright red base is revealed.

Specimens of bone marrow, imprints of the skin and sections stained with hematoxylin and eosin were shown.

DISCUSSION

DR. STEPHAN EPSTEIN, Marshfield, Wis.: Roentgen ray treatment of mycosis fungoides should be individualized. Some patients respond remarkably well to

small doses, whereas others require relatively larger single doses, such as 300 r, even in the pretumor stage. One might hesitate in this case to give further roentgen ray treatments on account of the low white cell count. In such a case, treatment with alpha rays is sometimes helpful. I mention this because ointments giving off alpha rays are now available, such as the radon ointment. Years ago I treated several patients with thorium X ointment, another means of applying alpha rays. The results were gratifying, in some instances, although only temporarily. An ointment containing at least 2,000 electrostatic units is advisable.

Dr. Emil Schleicher, Minneapolis (by invitation): This brings up the point I want to mention. The treatment is invariable, relieving no symptoms.

Dr. Stephen Rothman, Chicago: It is remarkable that the patient does not complain of itching and says that she has never scratched the lesions. On clinical grounds I doubt that this is mycosis fungoides.

Dr. L. H. Winer, Minneapolis: A microscopic section shows an infiltration of reticulum cells which are active—not so active, however, as in Hodgkin's disease of the skin. It was because of this biopsy of the skin that Dr. E. Schleicher, the hematologist, was called in to make studies of bone marrow, and he was able to observe these malignant cells both in the marrow and in imprints of the skin. The severe leukopenia that this patient has is something which was also explained on the basis of the malignant cells. Dr. Schleicher, will you explain the leukopenia?

Dr. Emil Schleicher, Minneapolis (by invitation): In my opinion this is not a case of mycosis fungoides but a low grade malignant reticuloendothelioma. The highly malignant type has been seen in Mrs. S., and, as will be remembered, leukopenia was the outstanding associated symptom. The leukopenia may be explained on the basis that the tumor cells or the reticulum cells replace the myeloid tissue or that the tumor is highly toxic to the myeloid tissue. In the latter case leukopenia results from arrest of the maturation of the myeloid tissue. At this point I wish to mention that the term "reticulocyte" has been used in the outline, a term which designates an immature red cell. The term "reticulum cell" is correct. In my experience the therapeutic application of roentgen rays and radium has given only temporary relief. This has been pointed out also by Dr. Epstein. We have seen complete disappearance of the cutaneous lesions as well as of tumors within twenty-four to forty-eight hours, and the symptoms did not recur at any time over periods of from one month to six months. It has been shown by serial biopsies that the tumor is not killed, that a small number of mitotic figures are demonstrable in the histologic preparations. On recurrence the tumor invasion is usually much more severe than it was before therapy. This has led to the belief that radiation, while suppressing the tumor growth, will either stimulate the tumor per se or bring a change in the surrounding tissue. As an example, I wish to cite the case of Mrs. S. Recurrence of the tumors was noted within four weeks after their retrogression. The histologic structure of the low grade malignant reticuloendothelioma or reticuloma is well presented in the histologic preparation shown today under the microscope. The lesion is not difficult to recognize, because of the extensive hyperplasia of the reticulum. Further, one has seen these reticulum cells, with their large elliptic or round nuclei and abundant light-staining cytoplasm, in the cutaneous imprint. Moreover, the bone marrow was demonstrated in the form of a histologic preparation, and, as will have been noted, the hyperplasia of the reticulum is in every respect malignant; at its periphery there is an inflammatory zone consisting of small lymphocytes, eosinophils and macrophages. The lesion in the marrow is exceedingly early. I am unable to state how soon the marrow will be completely replaced by this process.

Dr. Paul O'Leary, Rochester, Minn.: I still find chaulmoogra oil and fever therapy of help in treating patients with mycotic fungoides. The use of chaulmoogra oil was suggested by Lomholt, of Copenhagen, and I added the fever therapy to the program because it seemed to me that when used alone fever moderated the itching somewhat. It might be that I have unwittingly given this treatment to patients who have had the milder forms of mycosis fungoides, but

in any event the course of the disease has been slow after the treatment in all my cases. I agree with the patients who suggested that roentgen ray therapy seemed more efficient after the course of treatment with chaulmoogra oil and fever—evidenced by the rapidity with which the plaques melt out under lesser doses of roentgen rays.

DR. STEPHEN ROTHMAN, Chicago: I have been much interested in Dr. O'Leary's remark. On record is the case of a patient who for the last two years was completely free of signs and symptoms. He had clinically typical premycotic lesions and numerous large tumors. The histologic data also were typical of mycosis fungoides. He obtained as much roentgen ray irradiation as was permissible, but the lesions and tumors did not clear completely. Treatment with ethyl chaulmoograte was continued for several months. In the management of mycosis fungoides with roentgen rays alone, I never experienced such long periods without relapse. I should like to ask Dr. O'Leary what dosage he uses.

DR. PAUL O'LEARY, Rochester, Minn.: The chaumoogra oil is given intramuscularly in doses of from 2 to 6 cc. every day for approximately thirty injections while the patient is receiving five to eight hyperthermy treatments. I have given as much as 15 cc. of Chaulmestrol per day. I want to avoid giving the impression that mycosis fungoides is cured by chaulmoogra oil and hyperthermy, but I am convinced that it makes the disease less of a burden to the patient.

Synovial Lesion of the Finger. Presented by DR. L. H. WINER, Minneapolis.

Mrs. P. J. F., a white woman aged 57, two years ago had a similar lesion at the site of the present one. It disappeared spontaneously but recurred in the past six months and gradually enlarged.

On the dorsum of the terminal phalanx of the left middle finger, just distal to the terminal interphalangeal joint and to one side of the midline, is a globular cystic mass measuring 12 by 7 mm. It is 3 mm. in height. It is painless to pressure and white.

The patient also has arthritis of the fingers of the right hand, which are stiff. The lesion is being treated with roentgen rays.

DISCUSSION

DR. L. H. WINER, Minneapolis: I showed this patient because she also is being treated by a colleague for arthritis. This physician said that he sees 10 to 15 such patients a week and that the lesion is simply an enlargement of the capsule of the joint with gelatinous contents. He expresses the contents after piercing the capsule with a needle, and the joint gets well in a few days. My experiences have been quite the contrary. I have been treating such joints with roentgen rays, and they are slow in responding. Others have been excising the involved tissues with ulcers and draining sinuses resulting.

Chancroid? Presented by DR. S. E. SWEITZER, Minneapolis.

C. S., a white man aged 44, was admitted to the Minneapolis General Hospital on February 8. Four weeks ago, five days after exposure, he noticed a lesion on the dorsum of his penis. The sore was not painful and caused him no discomfort. The lesion gradually enlarged. Serologic tests for syphilis were weakly positive. A smear did not show the presence of Ducrey's bacillus. Cutaneous testing with an antigen prepared from a culture of Ducrey's bacillus and autoinoculation have been done. Dark field examination failed to show the presence of Treponema pallidum.

An examination revealed a large oval ulcer, 2.5 to 3 cm. in diameter, on the dorsum of the penis. There is crusting as well as a pustular discharge. There is moderate enlargement of the inguinal lymph nodes, which are painless and discrete.

DISCUSSION

DR. PAUL O'LEARY, Rochester, Minn.: About 1 case of chancroid a year is seen at the Mayo clinic. Last year Dr. Day and I saw a young married woman with chancroids of four days' duration. Her husband, a sailor, had a chancroid in January 1944, which was treated with a sulfonamide compound, and a rapid disappearance of the lesion followed. He returned home in September 1944, and five days after he arrived home his wife had lesions which were subsequently diagnosed as chancroids. She was intolerant of the sulfonamide compounds; hence penicillin was given, with a complete disappearance of the lesions. An examination of her husband did not reveal a lesion of any type on his genitalia; cultures of material from the prostate, stimulating irrigations of the urethra and manipulation failed to obtain a positive culture for Haemophilus ducreyi. I feel certain that the wife had no extramarital exposure. Women without demonstrable ulcerations have been found to be carriers of H. ducreyi, but it is rarely that a man has been thought to be a carrier when he has no obvious lesions of the genitalia.

A Case for Diagnosis (Sporotrichosis?). Presented by DR. J. F. MADDEN, St. Paul.

D. R., a school boy aged 12, skinned a rabbit on Nov. 1, 1944. About a week later an abscess appeared on the dorsum of the right index finger, over the first phalangeal joint. This was incised by his local physician. At intervals of a few days several nodules and abscesses began to appear and extend up the arm. Some of these ulcerated, and others remained as hard painless marble-sized red nodules. At present there are two irregular olive-sized fungating lesions on the dorsum of the hand and several nodules varying in size from that of a marble to that of an olive, on the forearm and the arm, extending from the fingers to the shoulder. The lesions are asymptomatic. There is also an olive-sized ulcer on the lateral surface of the middle third of the left leg. There was no history of previous injury to the hand. The patient feels well, and his temperature is normal. Three agglutination tests for tularemia were negative, the last one being made the first week of January 1945. The Wassermann test of the blood was negative. The Mantoux test with a 1:1,000 solution of old tuberculin elicited a negative reaction. A biopsy specimen was shown. Fungi were not found in fresh preparations made with sodium hydroxide.

DISCUSSION

DR. STEPHEN ROTHMAN, Chicago: This morning Dr. Madden showed me the culture tubes, but it was impossible to identify the colonies, because of heavy bacterial contamination. Clinically, I think, the best diagnosis is sporotrichosis.

DR. FRANCIS LYNCH, St. Paul: Have iodides been given?

DR. J. F. MADDEN, St. Paul: No.

DR. C. D. FREEMAN, St. Paul: I do not believe that one may contract tularemia in Minnesota during the month of February since all the rabbits infected with tularemia are long since dead. I am definitely satisfied that this is a case of sporotrichosis.

DR. H. E. MICHELSON, Minneapolis: Sporotrichosis can be found in plants. Why is it so rare in human beings?

DR. STEPHEN ROTHMAN, Chicago: Apparently sporotrichosis is not widespread in this country. It is rather common in Europe. Many cases have been reported in which the infection could be related to an injury incurred by walking barefooted in fields and among bushes or by pricking the skin of the finger on thorns of plants. The formation of real abscesses is rather characteristic.

DR. J. F. MADDEN, St. Paul: Most of the lesions were abscesses, which were incised by his family physician.

LOS ANGELES DERMATOLOGICAL SOCIETY

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Feb. 13, 1945

Granuloma Annulare Disseminated Type. Presented by DR. SAMUEL AYRES JR.

N. T., a white girl aged 8 years, had an acute attack of urticaria at the age of 2 years. The present eruption, beginning seven months ago, was the next disease of the skin. The first lesions appeared on the buttocks. Mild itching was present at the onset, but now there is no itching. Lesions have appeared on the thighs and the trunk in the past two months.

The lesions are widely scattered, but they are most abundant over the medial portions of the buttocks. They are rather indistinct, pale pink areas. Some are as small as 6 mm. in diameter, and others are 2 cm. in diameter. They have a waxy appearance.

A patch test with tuberculin elicited a negative reaction. A rentgenologic examination of the chest did not show evidence of pulmonary tuberculosis.

The biopsy slide showed numerous epithelioid cells, a few plasma cells and an occasional Langhans giant cell. These cellular elements together with lymphocytes formed an infiltration of the dermis, presenting a picture consistent with granuloma annulare.

DISCUSSION

MAJOR EVERETT R. SEALS, M.C., A.U.S. (by invitation): Has any one followed granuloma annulare without any treatment long enough to determine the duration of the disease? Will the skin clear spontaneously after a time?

DR. SAMUEL AYRES JR.: I do not think that I have ever followed granuloma annulare without treatment over a long period, but I have seen cases in which the eruptions have been present for periods of months to several years, and I know that cases in which the disease has lasted for years have been reported in the literature. This particular type of eruption is uncommon and is not similar in its clinical appearance to the more familiar type that occurs in ring formation on the hand.

A Case for Diagnosis (Pigmented Basal Cell Epithelioma or Melanoma?). Presented by DR. JOHN D. ROGERS.

Mrs. V. K., a white woman aged 59, has a brownish black, slightly elevated, irregular dime-sized lesion on the right cheek. In the lower margin is a small firm elevated lesion about 3 mm. in diameter which shows some telangiectasia over its surface. The nodular lesion is about eight weeks old. The flat pigmented area has been present for twenty years. There has been no change in the past three years. There has been no treatment.

DISCUSSION

DR. M. E. OBERMAYER: I do not feel that the tumor is a melanoma, but I believe that the dark lesion is a hyperpigmented seborrheic wart, from which a basal cell epithelioma has developed. I suggest a punch biopsy of the two types of lesions present in this area. Then let the therapeutic measures indicated by the microscopic aspects be followed.

DR. SAMUEL AYRES JR.: I think that the members could argue at length and still have diverse opinions, but it seems to me that since this person has had a black lesion all her life and since some growth has recently taken place in that area every precaution should be taken. I do not see what objection there is to excising the entire area with a cutting cautery. There is no point in taking

specimens for biopsy here and there. It would not disfigure the patient's face to have the entire lesion taken out. I cannot understand why it would make any difference if procaine hydrochloride were injected around the infected area. Using the infiltration method of inducing anesthesia could make no difference, one way or another.

DR. H. P. JACOBSON: On clinical grounds, I question the diagnosis of basal cell epithelioma. According to the patient's history, she has had the pigmented patch on the temple for at least twenty years. It is a sharply marginated, nonelevated, deeply pigmented, irregularly shaped plaque. Extending from the lower border is a hemispheric nonpigmented nodule, approximately 1 cm. in diameter. This is of recent origin. The morphologic picture, together with the clinical history, suggests a diagnosis of melanotic nevus and amelanotic melanoma. The therapeutic indications are definite. I cannot stress too emphatically the need for radical management of cases such as this. I have had the misfortune to see many tragedies resulting from conservative treatment of melanotic lesions, and, unfortunately, some of these tragedies have resulted from conservative treatment on the part of dermatologists. Some of the members are naturally much concerned with cosmetic results. In the treatment of malignant lesions, however, such considerations, in my opinion, are entirely unjustified. The only desideratum, which should be the dermatologist's guide, must be the destruction of the malignant lesion plus a safe zone of healthy tissue surrounding it. Melanotic malignant growths are radioresistant. The only logical and safe therapy requires radical surgical removal with the actual cautery under general anesthesia. I am opposed to infiltration anesthesia in cautery excision of these lesions.

DR. J. WALTER WILSON: I did see the case Dr. Jacobson refers to, but I should like to go on record as believing that procaine anesthesia is not harmful.

DR. W. H. GOECKERMAN: I think that Dr. Jacobson is probably too much inclined to castigate the dermatologist. Every dermatologist worthy of the name is fully cognizant of the vicious character of certain pigmented lesions. While the detailed approach in treatment may vary somewhat, the aim is certainly to eradicate drastically any pigmented lesion that has the possibility of becoming a melanoma. On the other hand, I, too, feel that it is difficult clinically to be sure whether or not a pigmented lesion is already a melanoma if there is as yet no definite clinical evidence of growth. One of my colleagues, with much experience in the field of cancer, emphasizes this feature by saying that in his opinion if the Cohnheim theory of misplaced cells applies to any form of cancer it does so in the case of lesions that become melanomas. In fact, he feels that all of them are definitely malignant, even when not active. It is certainly wise, therefore, to approach any pigmented lesion with all possible caution.

NOTE.—A later report on a biopsy specimen from the lesion showed it to be a malignant lesion—a melanoma.

Liquefying Nodular Panniculitis. Presented by DR. SAMUEL AYRES JR.

G. C., a white woman aged 49, approximately three years ago had about fourteen lesions similar to the present ones. Just prior to the onset of the present lesions she lost almost 35 pounds (16 Kg.) and had periods of nausea lasting for several days. Such an attack usually came just before the onset of a new lesion. She was free of lesions for one year until four months ago, when the present group began to develop. The first of these was on the right arm. All lesions follow a similar course. At first the patient feels a deep, slightly tender, thick, round lump which seems to be in the subcutaneous tissue. Nothing is visible. The process gradually enlarges and reaches the surface, forming a dull red elevation. This becomes fluctuant, breaks down, discharges and finally heals, leaving a depressed soft scar.

On the lateral surface of the right arm there is a new lesion, a slightly fluctuant, oval, brownish pink area, about 1 cm. in diamenter. Surrounding it

is a deeply infiltrated area, apparently involving the subsutaneous tissue. A similar lesion is on the lateral surface of the right thigh. It is an area of infiltration, about the size of a dime, which is not discolored and is only slightly elevated. Close to this is a pitted scar, also about 1 cm. in diameter. On the anterior surface of each shoulder and over the buttocks and the posterior surfaces of the thighs are numerous dime-sized depressed soft scars.

A tuberculin patch test was faintly positive after five days.

DISCUSSION

DR. H. P. JACOBSON: I agree fully with the opinion expressed by Dr. Ayres. The differential diagnosis in this case rests between three possibilities: (1) the diagnosis as presented, (2) subcutaneous fibromas and (3) sarcoids. Subcutaneous fibromas and sarcoids usually show no tendency to suppurate. The presenting lesions, in contrast, show evidence of suppuration, followed by healed depressed scar formations.

DR. W. H. GOECKERMAN: I should like to suggest the diagnosis of erythema induratum. Bazin emphasized in his original paper describing the disease that not all lesions of erythema induratum become necrotic and that these lesions need not necessarily predominate on the legs. My clinical experience agrees with this. Often too much emphasis is laid on the necrotic lesions occurring on the calf. A biopsy should be of help, although even it may not clearly distinguish between liquefying nodular panniculitis and erythema induratum.

DR. SAMUEL AYRES JR.: In checking over the literature, I found that a case was reported by Dr. Bertram Schaffer in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**38**:535, 1938). At that time he expressed the opinion that it was a rather new entity, and he differentiates it from the relapsing febrile nonsuppurative panniculitis (Weber-Christian syndrome). The lesions do not suppurate. In his case there was relatively little fever and at times none at all. Nearly all the lesions suppurated. One should also consider tuberculous gumma. The lesions in such cases are more chronic in their ulcerative phase. In this case, every individual lesion takes three or four months, after the time it is first palpated, to come to the surface and suppurate. Then it heals rapidly and is followed by a depressed scar as if some destruction of the underlying fatty tissue had taken place.

Anetoderma Erythematosum of Jadassohn (Dermatitis Maculosa Atrophicans). Presented by DR. M. E. OBERMAYER.

H. F., a woman aged 32, has a healed tuberculous pulmonary lesion, diagnosed by roentgenologic examination when she was 19. She had a complete hysterectomy four years ago. The present cutaneous lesions began when the patient was 6 years old, after tonsillectomy. The first lesions were on her neck. One by one they came for a period of two years. The present "marks" have remained unchanged. No new lesions came until two years ago. Then they began to appear on chest, back, arms and legs. At first they were red, and gradually they underwent a scarlike change.

Individual lesions vary from 5 to 15 mm. in diameter. They are irregularly distributed on both sides of the neck and over the sternum, the extensor surfaces of the arms, the flexor surfaces of the forearms, the lower part of the back and the extensor surfaces of the thighs. The newer lesions are slightly erythematous, while the older ones are whitish and show a cigaret-paper-like wrinkling. The macules on the neck are distinctly depressed and arranged with their long axes in the direction of the lines of cleavage of the skin. Most of the lesions on the forearms are slightly elevated, soft and compressible, so that a hernia-like impression is gained from palpation.

The Kolmer and Kahn reactions of the blood were negative.

A biopsy specimen from one of the most recent erythematous macules on the right thigh showed an epidermis of normal thickness, with a fluffy corneal

layer and an absence of the rete processes. The corium was edematous, and the nuclei of the connective tissue cells were increased in number and size. The blood vessels were dilated, and a moderate amount of perivascular lymhocytic infiltration was present. The connective tissue fibers appeared somewhat homogenized. They were irregularly arranged and took the stain poorly. Sebaceous glands, sweat glands and lanugo hairs were normal.

DISCUSSION

DR. HAL E. FREEMAN: This eruption apparently is what I call a primary macular atrophy of the skin as opposed to secondary atrophies which follow other processes.

DR. M. E. OBERMAYER: I agree with Dr. Freeman that this rare disease belongs to the group of primary macular atrophies; for, although the beginning of the process is of an inflammatory nature, the inflammation is an inherent part of the entity, and the atrophy does not follow an inflammatory process of a different kind. The interesting feature of anetoderma erythematosum is its characteristic course, which is made up of three stages, the initial erythematous macular stage, the erythematous annular stage with central atrophy and the final atrophic stage with the hernia-like development. Another little known feature of the disease is the fact that the consistency of some of the hernia-like lesions is caused by the formation of fatty tissue in the dermis. This eventually replaces the degenerated connective tissue fibers.

A Case for Diagnosis (Maculosquamous Eruption Resembling Lupus Erythematosus?). Presented by DR. M. E. OBERMAYER.

J. M., a white man aged 35, had an eruption soon after birth. The first lesions were two small brown "spots," which gradually enlarged, over many years. A few new lesions formed. Since he was 18 the process has remained stationary. The only subjective symptom has been an occasional slight itching.

There were about five erythematosquamous plaques, measuring 1 to 2 cm. in diameter. They have irregular contours and a surface which has fine scales. The lesions are almost level with the skin. There is no sign of atrophy.

The biopsy specimen showed a thin epidermis, which varied in thickness The irregular stratum mucosum had intercellular and intracellular edema and bulging rete pegs. The basal cell layer was intact. There was follicular plugging as well as slight parakeratosis. The dermis appeared filled with large lymph spaces and abnormally dilated blood vessels. A diffuse lymphocytic infiltrate was present all through the middle and the upper parts of the dermis where it blended with the epidermis. Many adenomatous sebaceous glands were present all through the dermis; the sweat glands and the subcutaneous tissue were normal.

DISCUSSION

DR. PAUL D. FOSTER: It is unusual to see a lesion of this type remain for such a long time. Clinically and microscopically the diagnosis of lupus erythematosus must be made. If the history is true, this patient is the youngest person with lupus erythematosus I have ever seen.

DR. W. H. GOECKERMAN: I want to support Dr. Obermayer unhesitatingly in his suspicion of lupus erythematosus. The history may be disregarded. The clinical appearance is typical of lupus erythematosus, and with the supporting evidence in the microscopic picture I think that one need not hesitate in making that diagnosis.

DR. SAMUEL AYRES JR.: The patient said that he had had the lesions all his life. They must be nevi of some sort.

DR. M. E. OBERMAYER: This case was presented "for diagnosis" in order not to bias the judgment of the members. I think that the clinical appearance of the lesions as well as the microscopic aspects point toward a diagnosis of chronic

discoid lupus erythematosus. Yet, the course of the disease is most unusual. It developed right after birth, evolved extremely slowly and then remained stationary for almost twenty years without producing definite clinical atrophy. This behavior, together with the unilateral localization, made me consider an atypical form of nevus unius lateris.

A Case for Diagnosis (Contact Dermatitis?). Presented by DR. CLEMENT E. COUNTER.

D. A., a white man aged 28, has had hives recurrently three times a year since he can remember. There has been no urticaria in the last ten months. The present eruption began about eight months ago. It has been persistent ever since. There have been some fading and some recurring, but given papules persist, even though they are redder at some times than at other times.

The patient's general appearance is excellent. The red papular eruption is distributed over a limited area around the hips. In fact, papules are found only on the area covered by bathing trunks and on the medial surfaces of the arms. Individual lesions are smooth and red and raised about 1 mm. above the skin. All lesions are discrete. They average 3 mm. in diameter.

The biopsy specimen showed some perivascular round cell infiltration, evidencing a nonspecific inflammatory reaction. There was an occasional mast cell.

Ultraviolet rays have been used in mild erythema doses.

DISCUSSION

DR. H. P. JACOBSON: The eruption is peculiarly limited around the hips to the area corresponding to the borders of his shorts. I am inclined to think that it might be a contact dermatitis, either from the washing soap or the fabric of his underwear.

DR. W. H. GOECKERMAN: I think that this eruption is urticaria papulosa. If rubbed, the lesions become turgescent. The patient has had urticaria. The clinical picture is rather typical of that special kind of urticaria.

DR. M. E. OBERMAYER: I am certain that this case is one of papular uriticaria. The presence of small vesicles on the top of some of the lesions makes it likely that the eruption is the type of papular urticaria known as strophulus.

A Case for Diagnosis (Lichen Planus?). Presented by DR. IRVING BANCROFT.

V. W., a Negro woman aged 32, three years ago began to have an itching eruption under her arms. The same eruption appeared under the chin and on the back of the neck about two years ago. Similar lesions developed on the medial sides of the arms about two years ago.

The patient is obese. There are hyperpigmented areas under the arms. Excoriations are present. In both axillary areas are finely furrowed and scattered papules. There are also areas of lichenified scattered papules on the front and on the back of the neck. The right elbow and both forearms have similar areas. Hyperpigmentation is present in the older eruptions.

Various ointments have been used locally, and bismuth subsalicylate in oil has been given intramuscularly.

The Wassermann reaction of the blood was negative. No fungous elements were demonstrated by direct microscopic examination of scales. The biopsy specimen showed only round cell infiltration and other signs of nonspecific chronic inflammatory process.

DISCUSSION

DR. H. C. L. LINDSAY: The lesions on this patient do not look like those of lichen planus, but they do resemble patches of neurodermatitis.

DR. M. E. OBERMAYER: The disease is more likely to be lichen chronicus simplex than lichen planus. Differentiation in a dark-skinned person is not possible without biopsy.

MAJOR EVERETT R. SEALS, M. C., A. U. S. (by invitation): That is something readily seen in Houston, Tex. It is almost always found in Negroes. It is called neurodermatitis. It does not respond to any kind of treatment. It lasts more or less all the year around, but it is worse in the summer. Sweating is a factor in producing it.

Urticaria Pigmentosa of Bullous Type. Presented by DR. PAUL D. FOSTER.

S. A. is a girl 4 months old and is the only child. Her parents are well. The eruption has existed since birth. The reddish marks develop "blisters." When a "blister" breaks, the erythematous lesion remains. She has these lesions on the extremities, the body and the head. Apparently they cause no pain.

The baby's general appearance is healthy and well nourished. The lesions are in multiple areas on the body, the legs, the arms and the head. They are about 2 cm. in diameter and irregularly round. All are pigmented a dark brown. The surfaces of the lesions have prominent follicular openings, producing the appearance of an orange peel. Some lesions have tense bullae present.

The biopsy specimen showed a thinned epidermis and an infiltration or replacement of the cutis by cells which were suggestive of nevus cells. The pigment was heaviest just at the basal layer of the epidermis.

DISCUSSION

DR. PAUL D. FOSTER: The slide is strongly suggestive of a nevus, and the fact that the child was born with this disease strongly suggests the diagnosis of a nevus. It is the first case of this type that I have ever seen.

DR. M. E. OBERMAYER: Vesicle and bulla formation in cases of urticaria pigmentosa is extremely rare. Yet there is no reason for denying the possibility of bulla formation in any case of inflammatory dermatosis when the exudative process happens to be of an unusually high degree. I think that this child has a bullous form of urticaria pigmentosa.

DR. H. P. JACOBSON: The lesions presented by this child are peculiar tumor masses, which I have never seen. I have never observed such lesions in connection with urticaria pigmentosa. It is possible that these are lymphangiomas, associated with intense inflammatory cellular reactions.

Keratosis Palmaris et Plantaris. Presented by DR. SAMUEL AYRES JR.

C. B., a white child aged 9 years, has had on eruption for five years. At first only two fingers were involved. Later the disease extended to include the palms and the soles, and it has been persistent. No other member of her family has similar thickening of the palms and the soles.

The eruption is limited to the palms and the soles except for slight involvement on the anterior aspects of the ankles, the knees and the elbows. One year ago her feet were so badly broken out that it was necessary for her father to carry her into the office, and at that time the palms and the soles were extremely hyperkeratotic. Greater thickness was present on the backs and the medial aspects of the heels. With regard to the palms, the eruption was particularly bad on the tips of the fingers and on the hypothenar prominence. There was fissuring. Areas on the ankles, the knees and the elbows were less thickened. They were slightly erythematous, dry and scaly. There were ill defined dryness and roughness on the arms and the legs, with slight follicular hyperkeratosis. The hair on the forearms near the elbows is longer than that usually seen on children's extremities.

Normal amounts of nonprotein nitrogen and uric acid were present in the blood. No fungous elements were present in scrapings from plantar and palmar lesions.

Vitamin A has been given for the last year. During part of that time 150,000 units was given daily. Sixteen roentgen irradiations were given at weekly intervals.

Seventy-five roentgens was given to each lesion at each treatment. Local medications have included ointments containing juniper tar, salicylic acid, anthralin ointment and simple bland creams. The eruption has improved, but the hyperkeratosis continues.

DISCUSSION

DR. MILTON GOLDMAN (by invitation): I was interested in the possible functional nature of this eruption. The aunt and the grandmother on the maternal side had asthma. The mother recently had eczema. I thought of the possibility of a functional dermatosis.

DR. M. E. OBERMAYER: I agree with Dr. Goldman. Keratosis plantaris is hardly ever present in the form of sharply circumscribed plaques. I have never seen a case in which such plaques were located also at the sides of the feet. The disease is more likely to be a hyperkeratotic form of dry neurodermatitis.

DR. RICHARD L. SAUNDERS (by invitation): This case impressed me as one of psoriasis of the palms and the soles.

DR. A. FLETCHER HALL: I agree with the diagnosis of psoriasis. Biopsy would prove it.

Neural Leprosy (Maculoanesthetic Form?). Presented by DR. MOLLEURUS COUPERUS.

E. B. is a young Mexican woman aged 19. Her father died of alcoholism. Her sisters and her mother are living and well. None of her family or near relatives have had any cutaneous disease. She entered the United States one year ago. Four years ago a small red spot appeared on the right leg. Its enlargement has been gradual since then. A few small red spots have appeared on the other leg and the thigh during the past month. The patient has noticed that there is no sensation of pain in certain parts of the large area on the leg when the area is scratched. She is underweight.

On the outer aspect of the right leg, covering the lower two thirds and almost encircling the leg in the middle, is an erythematous plaque which is macular in type except at the periphery, where there is a slight elevation suggesting minute nodules. The entire lesion is slightly scaly, and there is atrophy in the central part of the patch. There is no sensation of touch or pain in this area. Outside the large patch as well as in a few areas on the trunk and on the opposite leg there are pea-sized erythematous macular areas. Some of these are hypersensitive, and some are anesthetic.

The Wassermann reaction of the blood was negative. Mycobacterium leprae was not found either in repeated nasal smears or in repeated smears of material obtained by puncture from the lesion on the leg.

The biopsy specimen showed thinning of the epidermis. In the upper part of the cutis there was considerable dilatation of the blood vessels, and here, as well as through the entire cutis, there were focal aggregates of epithelioid cells associated with small round cells and fibroblasts. Some of the infiltrate surrounded nerve fibers.

DISCUSSION

DR. M. E. OBERMAYER: I agree with the diagnosis, though I had no opportunity to study the section. That the patient came from Sinaloa is significant because that state has the highest incidence of leprosy in Mexico. I should like to perform the Mitsuda-Rost test on this patient. As I had the opportunity to observe during my recent visit to Mexico City, the prognostic significance of this test is paramount. A positive reaction indicates a satisfactory allergic response and is encountered in practically all cases of tuberculoid lepra. The course of the disease will remain relatively benign, and specific therapy is apt to bring improvement. A negative reaction indicates a lack of allergic response and is encountered in the lepromatous forms of the disease. The test is performed by intracutaneous injection of an antigen derived from maceration of tissue rich in

lepra bacilli and is read in the same way as a tuberculin test. Dr. Fernando Latapi, professor of dermatology at the National University of Mexico, not only demonstrated the Mitsuda-Rost test for my benefit but has also supplied me with antigen. From what I have learned in Mexico it may be said that a correct diagnostic interpretation of a case of leprosy without the aid of the Mitsuda-Rost and histamine tests is a thing of the past.

DR. HAL E. FREEMAN: In the few cases of leprosy that I have seen, erythema has not been present in the anesthetic areas. Just looking at the process in this patient, one would think of the clinical picture of Kaposi's idiopathic hemorrhagic sarcoma.

DR. SAMUEL AYRES JR.: Were Hansen's bacilli found in the tissue?

DR. MOLLEURUS COUPERUS: This form of leprosy often shows no Hansen's bacilli in biopsy specimens or in material obtained by superficial punctures of the skin. I do not believe that any other diagnosis is possible in this case. The erythema is greatest near the advancing border of the lesion, while in the center it is much less. This is not uncommon. From a clinical standpoint this form of leprosy has a fairly good prognosis with modern therapy. I shall be happy to have Dr. Obermayer perform a lepromin test on this patient.

NOTE.—A histamine test of this patient failed to elicit an erythematous flare in the area of the cutaneous lesion but produced such erythema elsewhere. Dr. Obermayer performed the Mitsuda-Rost (lepromin) test, which elicited a positive reaction.

Localized Hyperhidrosis. Presented by DR. SAMUEL AYRES JR.

R. S., a man aged 59, has had hay fever most of his life during the summer.

His hyperhidrosis began about thirty-five years ago, after an illness involving an appendectomy and at the same time the incision of an abscess near the angle of the right jaw. Ever since that time his right cheek has broken out with profuse perspiration a few minutes after eating. Such foods as chocolate cake particularly stimulate this perspiration. The attack usually comes on within ten minutes after eating and persists for five to fifteen minutes. The perspiration drops off his chin, necessitating the use of a handkerchief.

The patient ate a lunch just before being observed at the clinical presentation. Much clear fluid accumulated on the right cheek in a defined round area about 6 cm. in diameter. Enough fluid accumulated to run down and drip off the chin. The flow of the fluid stopped in five minutes. Only slight erythema of the right cheek was left to show where the fluid had come from.

Positive reactions of the skin were not produced by any of the one hundred and fifty food pollen extracts tested.

DISCUSSION

DR. PAUL FOSTER: This case represents a vasomotor imbalance brought on after an operation for a deep abscess thirty-five years ago. At that time a large incision was made that went deep into his neck, and immediately afterward the right side of his face started to perspire. I have seen 2 cases in which the sympathetic cervical ganglions had been anesthetized with procaine. In each instance there was localized increase of perspiration like that present in this case.

DR. ANKER JENSEN: I believe that this man has some extra parotid tissue close to the surface of the skin. His condition may be analogous to endometriosis.

DR. SAMUEL AYRES JR.: The fluid has the appearance and the consistency of perspiration. This sweating develops only after the patient has eaten, and especially after he has eaten rich food. One of my classmates had a similar hyperhidrosis when eating peanuts or chocolate. On scratch tests this patient did not show hypersensitivity to food proteins, but he has had hay fever for many years, suggesting an allergic background. The discomfort comes from the necessity of mopping his face with a cloth after every time he eats.

MANHATTAN DERMATOLOGIC SOCIETY

George M. Lewis, M.D., *President*

Wilbert Sachs, M.D., *Secretary*

Feb. 13, 1945

A Case for Diagnosis (Eruption of Chest and Back, Aggravated by Sunlight). Presented by DR. JACK WOLF.

R. M., a woman aged 24, is presented with an eruption of approximately four years' duration, which began in the presternal region and gradually spread peripherally until it reached its present size. Satellite lesions have continued to appear. The only relevant observation that the patient has made is that the eruption becomes more acute on exposure to the sun but that it does not necessarily spread as a result of such exposure.

On examination the patient presents a diffuse mottled erythematous eruption, forming a more or less reticulated pattern and extending from the supraclavicular regions down to the inframammary area. Laterally it extends as far as the midclavicular line. The individual lesion is barely perceptible to the touch, and the elevation can be seen only when observed at the proper angle.

A piece of tissue removed from one of the more prominent lesions revealed only a moderate interstitial and parenchymatous edema in the upper and middle parts of the corium, with superficial dilatation of the vessels. No histologic diagnosis could be made.

DISCUSSION

DR. FRED WISE: I suggest a diagnosis of atypical seborrheic dermatitis, and I should use resorcinol lotion as a therapeutic test.

DR. HERMAN SHARLIT: I agree with the suggestion of Dr. Wise.

DR. MAX SCHEER: I, too, agree with the diagnosis, especially on account of the lesions between the shoulder blades, which look much like seborrheic dermatitis to me.

DR. DAVID BLOOM: This patient shows tiny papules in linear arrangement, which I have seen in a case of ectodermal dysplasia of the anhidrotic type and which has also been described by MacKee in his case. The lesions were located on the neck in those cases and were supposed to be due to degeneration of sebaceous glands. I do not know whether these lesions have any connection with the eruption for which the patient was presented.

A Case for Diagnosis (Poikiloderma Vasculare Atrophicans?). Presented by DR. FRED WISE.

F. S., a woman aged 26, was referred by Dr. Harold N. Cole, of Cleveland, with an eruption of the body which she has had practically all her life. The family history is essentially noncontributory. The patient states that she used to perspire on her face and her back and under her arms and that she still perspires on her face and under her arms. She notes some perspiration on her palms during warm weather. She says that in hot weather she is uncomfortable and that her face gets flushed, although she does do some work.

An examination revealed an eruption that is most extensive on the arms and on the legs down to below the knees, being almost confluent in those areas, and even up onto the buttocks, with large, fairly well circumscribed areas on the trunk. There are also confluent areas on the neck. There are two types of lesions, the one in the form of macular pigmented areas and the other in that of erythematous retiform areas with telangiectasia, atrophy and scaling. Some fine telangiectases are present on the cheeks. The mucous membranes, the nails and the teeth are apparently normal.

A roentgenologic examination revealed that the chest is normal. The basal metabolic rate was —7 per cent. The blood calcium was 12 mg. and the blood phosphorus 3.5 mg. per hundred cubic centimeters. At the time of her examination vitamin C was 0.3 mg. and plasma cholesterol 221 mg. per hundred cubic centimeters, and the hemogram was perfectly normal, with a white blood cell count of 7,500.

A histologic examination showed considerable keratinization of the epithelium, with epithelial pegs entirely absent. The basement membrane of the epithelium was intact. In the upper portion of the dermis was a considerable infiltration of lymphocytes and large round cells. There was also some collagenous degeneration of the connective tissue. Hair follicles and sweat glands were found in the deeper portion of the dermis. There were scattered collections of inflammatory cells similar to those already mentioned, especially around vessels. The elastic tissue appeared fragmented.

DISCUSSION

DR. HERMAN SHARLIT: What is the modern treatment?

DR. GIRSCH D. ASTRACHAN: This patient presented a pronounced diminution of vitamin C in the blood, the values being less than half of normal. That might provide a basis for therapy.

DR. WILBERT SACHS: I believe that all the members agree with the diagnosis. Some of these extensive eruptions eventuate into mycosis fungoides.

DR. MAX D. SCHEER: I think that a patient was reported on years ago in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY as having poikiloderma vasculare atrophicans and dying later of mycosis fungoides.

DR. WILBERT SACHS: That is not the only case; others have been reported.

DR. DAVID BLOOM: In the past few years I have had under observation several patients with this type of eruption. My impression is that it is due to a vascular disturbance of congenital origin. I am inclined to consider the occasional association with mycosis fungoides as coincidental.

Koilonychia. Presented by DR. ANTHONY C. CIPOLLARO.

E. R., a nurse aged 46, born in the United States, was the subject of an article which appeared years ago in the *New York State Journal of Medicine* (**30**:380 [April] 1930). She is now presented to show that the koilonychia has not changed in any fundamental way since then. She has had it since birth, and her mother and sister have a similar anomaly. While the patient was on duty in the operating room, contact with strong antiseptic solutions made the disease worse and caused pain. She is presented not only because this disease is unusual but also to reaffirm the fact that hereditary factors are the most pronounced in the causation of koilonychia.

DISCUSSION

DR. DAVID BLOOM: Koilonychia belongs to the nail dystrophies which are inherited according to a dominant mode.

DR. FRED WISE: It is an interesting observation that about five years ago an article was published in which it was stated that in practically every case the anomaly is associated with achylia gastrica. Dr. Cipollaro tells me that everything points against that probability in this case, although no analysis of the gastric content has been made. The fact that other members of the family have the same trouble suggests inherited disease. That angle should be investigated.

DR. HERMAN SHARLIT: The fact that a hereditary factor is involved does not mean that there is no remedy.

DR. ANTHONY C. CIPOLLARO: About 35 per cent of the cases of koilonychia reported in the literature have heredity and occupation as assignable causes. In about 30 per cent there were associated diseases. In none of the cases reported

were there any internal disturbances other than those which were coincidental. I did not perform an analysis of the gastric content in this case as there was no indication for it in a perfectly healthy patient. But I did determine the basal metabolic rate and made a blood count, and I searched for foci of infection or evidence of other congenital anomalies, without result.

A Case for Diagnosis (Toxic Erythema? Lupus Erythematosus?). Presented by DR. DAVID BLOOM.

M. Q., a woman aged 28, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 1, 1944, complaining of an eruption of seven years' duration. At that time the patient presented underneath the left breast a well defined dusky red plaque, semilunar in shape, in which the follicular openings were distinct as dark red spots. On the chest, over each supraclavicular region and on the back to the right of the left scapula there were plaques which consisted of ill defined, slightly raised, light red, edematous papules. After a few injections of bismuth subsalicylate the eruption improved considerably. The plaques became lighter, and some of them cleared almost entirely.

The patient now presents underneath the left breast a plaque which is light red, with follicular openings which are distinctly seen as pits. On the chest the plaques, consisting of light red edematous papules, are seen with difficulty, but in the supraclavicular regions the follicular openings are conspicuous and appear as being depressed. On the back the plaque can be distinguished only with difficulty.

The past and family histories were essentially noncontributory.

The urine and the blood count were normal. Biopsy revealed merely edema.

The Wassermann reaction was negative.

DISCUSSION

DR. FRED WISE: There is no evidence of any kind in support of the diagnosis of lupus erythematosus. In the Jadassohn Handbuch there are descriptions of various inflammatory follicular diseases associated with pitted atrophy of the follicular orifices.

DR. MAURICE J. COSTELLO: The follicular atrophy is of course the end result of the inflammation which preceded it. I observed for some time at Bellevue Hospital a patient, later reported on by Dr. Combes, who presented a picture somewhat similar to this, and I came to the conclusion that the eruption was an atrophic follicular form of lichen planus. I do not think that the history is consistent, but the eruption strongly resembled it clinically.

DR. DAVID BLOOM: The patient is presented for two reasons: first, for the remarkable improvement of the eruption which suggests a toxic erythema and, secondly, for the peculiar enlargement of the follicular ostiums.

A Case for Diagnosis (Vitamin C Deficiency? Schamberg's Disease?). Presented by DR. GIRSCH D. ASTRACHAN.

Z. L., a white boy aged 14, born in the United States, came to my office on Nov. 10, 1944, presenting an eruption on both legs and thighs of seven months' duration. The eruption began with a few lesions and spread gradually. It was composed of many scattered and closely set papular and macular lesions, many of which were purpuric in character, others being red to light brown. The patient complained of slow healing of the wounds and frequent infections of the skin. He was advised to drink large quantities of orange and tomato juices. Calcium gluconate and a proprietary exsiccated ferrous sulfate were prescribed. The eruption has improved during the last two months.

The patient now presents on both legs and ankles and the lower parts of the thighs an eruption composed of well defined, irregularly shaped lesions, varying

in size from that of a pinhead to that of a quarter, most of which are macular in character, others elevated and somewhat infiltrated. The color varies from yellowish brown to reddish brown. Several scars and a few lesions suggestive of slight atrophy are present on both legs.

A blood count on Oct. 23, 1944 showed 9,600 leukocytes, of which 42 per cent were neutrophils, 51 per cent lymphocytes and 6 per cent monocytes. The erythrocyte count was 3,860,000, the hemoglobin content 81 per cent and the platelet count 190,000. The bleeding time was three minutes and fifteen seconds, and the coagulation time was sixteen minutes. The vitamin C content of the blood plasma was 0.34 mg. per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood were negative. The sedimentation rate was normal. The icterus index was 7.5 units. The uric acid was 3.8 mg. per hundred cubic centimeters; dextrose, 75 mg.

Histologic examination of one of the lesions taken from the leg suggested the diagnosis of hemostatic dermatitis ("could possibly fit in with Schamberg's but not with Majocchi's disease." [Dr. Sachs]). Throughout the middle and upper parts of the cutis the vessels were somewhat dilated and the walls thickened. There was a moderate amount of telangiectasia. There was a focal small round and wandering connective tissue cell infiltration. Throughout the remainder of the cutis was a diffuse sparse fibroblast cell infiltration. The overlying epidermis was somewhat edematous in the lower portion, but otherwise it showed no important change.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: I do not believe that the patient suffers from a drug eruption. It is a purpuric eruption of some type, the exact nature of which I am unable to determine. Whenever I see a case of this type I have difficulty in differentiating between Schamberg's and Majocchi's diseases and purpura simplex. The vitamin C determination is a good thing to have, though I do not know how much significance it has from the standpoint of causation. If the vitamin C value is below normal, one can increase the intake, but I have not seen any effect of that on an eruption of this type.

DR. FRED WISE: I have never seen a clinical picture corresponding to this one. The variability of the lesions and of their size seem to me most unusual. One disease which could be eliminated is Schamberg's, as there is absence of hyperpigmentation in these lesions. From a distance the eruption simulates Majocchi's disease, but the histologic report fails to confirm the diagnosis since sacculation, hyalinization of the vessels and other criteria are lacking. The diagnosis seems to lie between purpura and dermatitis hemostatica. I see no reason why a healthy young boy with no signs of circulatory disturbances should have dermatitis hemostatica, and I therefore come to the conclusion that the eruption is an aberrant or atypical form of purpura.

DR. DAVID BLOOM: I should like to suggest the diagnosis of pigmented purpuric lichenoid dermatitis of Gougerot and Blum.

DR. FRED WISE: That does not resemble this. There are pinhead papules, and they are so small that one has to search for them.

DR. HERMAN SHARLIT: I suggest that some of the patient's blood be taken and hemolyzed and that the patient be given an intracutaneous injection of it. The blood on extravasation into the tissues may be causing a reaction *in situ*. This procedure may reveal such a status.

DR. WILBERT SACHS: Of this whole group of diseases, the one that can be diagnosed with ease by microscopic means is Majocchi's disease. As Dr. Wise said, one must have hyalinization of vessels, sacculation and other changes in order to make a diagnosis of Majocchi's disease. The other three may be very similar. Surprisingly enough, there is little to be seen microscopically in purpura. Schamberg's disease is more of an inflammatory process, while dermatitis hemostatica

is a long-standing process with telangiectasia and even some fibrosis. One could certainly rule out Majocchi's disease in this case on the microscopic features. I favor a diagnosis of dermatitis hemostatica, or possibly Schamberg's disease.

DR. GIRSCH D. ASTRACHAN: When I first saw this patient he presented real purpura with many small and large macular and papular lesions, purplish in color. He complained of slow healing of any wounds, and of frequent infections. The eruption improved greatly after the administration of calcium by mouth and the intake of large quantities of orange and tomato juices. I cannot make a definite diagnosis, but I do not think that one is dealing with a case of dermatitis hemostatica, because of the youth of the patient and because he has no varicose veins or circulatory stasis. The eruption is probably caused by vitamin C deficiency, and I shall try large doses of ascorbic acid.

A Case for Diagnosis (Trichokryptomania?). Presented by DR. HERMAN SHARLIT.

M. W., a girl aged 19, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 9, 1945, complaining of thinning and poor growth of her hair. She said that about one year previously a small bald spot appeared on the vertex of the scalp, which soon extended to involve the whole anterior aspect. After four or five months the hairs returned but did not grow beyond 1½ to 2 inches (about 4 to 5 cm.) in length.

At present the anterior aspect of the scalp and the parietal region show a thinning of the hair, which is not more than 1½ to 2 inches long. On the occipital and temporal regions the hair is normally thick and long.

The patient states that she has been treated by a commercial hair specialist, who advised her to brush her hair all day long. Recently she brushed her hair twice a day for ten minutes each time.

The past and the family histories are essentially irrelevant except that a younger brother is a mongolian idiot.

DISCUSSION

DR. MAURICE J. COSTELLO: I agree with the diagnosis. Sometimes a person will take instructions entirely too literally, and oftentimes merely rubs over small patches of the scalp, actually removing the hair by mechanical friction. These patients are of the hysterical type. In persons with an eruption such as this, which has persisted for ten years, I believe that other stigmas of hysteria could be demonstrated.

DR. DAVID BLOOM: The diagnosis of trichokryptomania can be made by exclusion. The bizarre picture of very short hair on the anterior aspect of the scalp with perfectly normal hair on the rest of the scalp and the history of vigorous daily brushing of the hair, together with the normal appearance of the hair under the microscope—all this justifies the diagnosis.

DR. FRED WISE: I do not agree with the diagnosis as presented, because of the uniformity of the alopecia and the absence of isolated patches resulting from recurrent plucking of the hairs on different areas of the scalp, as occurs in cases of genuine trichokryptomania in children. In this patient there is no evidence of a compulsion neurosis. I am more in favor of fragilitas crinium or some similar abnormality.

DR. WILBERT SACHS: Why is it that after so many years of rubbing the scalp, the hair is broken off and not lost? Years ago Dr. Wise reported a case of neurodermatitis of the forearms with complete alopecia.

DR. THOMAS N. GRAHAM: I think the fact that the involvement is so sharply outlined probably indicates that the patient used a brush only in that particular area. There is no loss of hair on the sides or the back of the scalp. These aspects would fit in well with a diagnosis of trichokryptomania.

Leiomyoma. Presented by DR. HERMAN SHARLIT.

R. C., a woman aged 28, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption on the right side of the chest of six years' duration.

On the right side of the chest above the breast there is an eruption of nodules which involve an area the size of a palm. The nodules are mostly lentil sized and reddish and are raised above the level of the skin. There are three pea-sized nodules which are extremely tender to pressure.

Biopsy confirmed the diagnosis of leiomyoma.

DISCUSSION

There was no discussion of this case.

Sarcoidosis. Presented by DR. DAVID BLOOM.

P. H., a Negro woman aged 30, came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 17, 1945, complaining of an eruption on the face and the neck of four years' duration. Her past and family histories were irrelevant except that from 1942 to 1944 she received intravenous and intramuscular injections at New York City Hospital, Welfare Island, in spite of a negative Wassermann reaction of the blood.

The eruption consists of a variety of lesions. On the glabella, at the outer aspect of the right eyebrow and on the tip of the nose and the upper lip, there are raised soft plaques, dark red-brown in color. The ear lobes and the ears are similarly affected. On the upper and the lower eyelids, in the canthi of the eyes, in the nasolabial fold and in the angles of the mouth, there are small round and annular lesions and groups of small nodules. On the lateral and posterior aspects of the neck there are depigmented linear lesions and groups of nodules.

A general examination revealed slight enlargement of the lymph nodes and the liver.

The Wassermann and Kahn reactions of the blood were negative. The blood count revealed anemia with eosinophilia and relative lymphocytosis (hemoglobin, 65 per cent; erythrocytes, 3,900,000 and leukocytes, 6,100, with 34 per cent neutrophils, 8 per cent polymorphonuclear eosinophils, 1 per cent basophils, 12 per cent monocytes and 41 per cent lymphocytes, with an occasional atypical cell). The sedimentation rate was greatly increased (62 mm., instead of 15 mm., an hour). A roentgenogram of the chest showed considerable nodulation at the hilus of each lung with small lymphoid deposits in the central pulmonary field. The thickening extended and diminished toward the periphery. There was otherwise no evidence of recent parenchymatous infiltration. The central thickening and nodulation were such as might well be observed with sarcoidosis. Tuberculin in a dilution of 1:10,000 elicited a negative reaction. Biopsy confirmed the diagnosis of sarcoid.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: There are some interesting features in connection with this type of sarcoid. A patient, especially one of the Negro race, with so much evidence of the disease diagnosed as sarcoid, is a candidate for miliary tuberculosis. I recall a husky, 6 foot (182 cm.) Negro with nodular lesions scattered all over the body, diagnosed both clinically and histologically as sarcoid, who died a year or two later of miliary tuberculosis.

DR. MAURICE J. COSTELLO: The roentgenographic picture of sarcoidosis closely resembles that of acute miliary tuberculosis, and I would be better satisfied in those cases if the diagnosis were proved correct post mortem. It is almost impossible to distinguish roentgenographically between acute miliary tuberculosis, carcinomatosis and pneumonoconiosis.

DR. DAVID BLOOM: My conception of this type of eruption, seen frequently in the Negro, is that it is an attenuated type of tuberculosis associated with a high

immunity. Many of these patients get entirely well with supportive therapy and some without any therapy at all.

Pyoderma Treated with Penicillin Ointment. Presented by DR. GEORGE M. LEWIS.

H. D., a white man aged 43, came to the New York Hospital on Nov. 4, 1944, with a swollen, exudative, erythematous and pustular eruption of the fingers of both hands, more severe on the left hand. A diagnosis of pyoderma was made.

A similar eruption had been present in 1933 for over five months before it responded to roentgen ray therapy. Cultures on blood agar revealed Staphylococcus aureus and hemolytic streptococci.

Treatment at first consisted of wet dressings and applications of ammoniated mercury ointment. There was some temporary improvement, with prompt relapse when treatment was discontinued. Treatment with penicillin ointment (400 units per gram) was begun on January 29. The response was favorable and rapid.

DISCUSSION

DR. HERMAN SHARLIT: What is the opinion of Dr. Lewis as to the stability of penicillin in the ointment? I have heard conflicting reports. On the other hand, there have been cases of sycosis presented in which the eruption was considered cured by this agent.

DR. MAURICE J. COSTELLO: I have heard that penicillin ointment remains stable for several months if kept in the refrigerator.

DR. THOMAS N. GRAHAM: I saw this patient several times, and I can vouch for the severity and persistence of the eruption. It was treated by many other measures without benefit, and the favorable response to penicillin ointment was most striking.

NEW ENGLAND DERMATOLOGICAL SOCIETY

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Feb. 14, 1945

Colloid Degeneration of the Skin. Presented by DR. JOSEPH GOODMAN, Boston.

M. R., an Irish housewife aged 62, presented a lesion of the forehead of four months' duration. At the onset there was a small reddish papule. This gradually increased in size, and similar lesions formed at its periphery.

On the left side of the forehead, there is an area 2.5 cm. in diameter consisting of yellowish translucent nodules 2 to 3 mm. in diameter surrounded by flat yellowish macules which are 1 mm. in diameter.

The results of the examination of the blood and the urine were within normal limits. The Kahn and Hinton reactions of the blood were negative. Histologic sections confirmed the diagnosis of colloidal degeneration of the skin.

DISCUSSION

DR. WALTER F. LEVER: The slide showed considerable degeneration of the collagen and elastic fibers. They were matted together into a structureless mass. I think the appearance of the slide was consistent with the diagnosis of colloid degeneration of the skin.

DR. BERNARD APPEL: It seems to me that it might be worth while to mention the clinical picture that one gets by looking at the lesions which at first glance present a pale orange-yellow color. The translucence and the color of the lesions suggest a xanthomatous tumor. It might be interesting to speculate on the relationship between the colors. Here is a tumor which, seen microscopically, contains

no cells which can be considered to be xanthomatous in nature, and yet the color is suggestive of a xanthomatous infiltration. The question arises as to the origin of this color. It might be of some value to try to explain the interesting physical character of the lesions.

Lichen Planus Hypertrophicus. Presented by DR. LEO KORETSKY, Chelsea, Mass.

C. F., a 50 year old white American housewife, presents pruritic lesions of the axillas, the neck and upper portions of the gluteal fold of one year's duration.

Scattered in the axillas and over the neck, there are shiny papular lesions and patches which have a deep purplish color. At the axillary portions bilaterally on the chest, there are crescent patches consisting of purplish and brown scaling lesions. There is a similar eruption in the upper portion of the gluteal fold.

Urinalysis on January 22 revealed fifteen hyaline and granular casts per high power field; on January 29 the results of an examination were within normal limits. The Hinton, Wassermann and Kahn reactions of the blood were negative. The histologic examination confirmed the diagnosis of lichen planus.

Two treatments with mercuric succinimide and one with bismarsen have produced no change in the lesions.

DISCUSSION

MAJOR EARL A. GLICKLICH: The lesions which were in the axillary fold gave me the impression that they looked somewhat like those I have been seeing among the military personnel. The multiple excoriations of the forearms did not resemble lichen planus. She is rather an obese woman, and I believe the same type of reaction can be seen in one who wears a tight brassiere from contact in that area, which with moisture may produce a contact dermatitis.

DR. JACOB H. SWARTZ: There were lesions in the mouth which were typical of lichen planus.

DR. FRANCIS M. THURMON: I thought the configuration of the lesions was a bit unusual for an out and out lichen planus. Certainly the color and the thickening of the lesions were suggestive of lichen planus, but when I looked at the microscopic section and saw the bandlike arrangement of infiltration it was typical of or consistent with lichen planus. I believe the greater part of the eruption was lichen planus, with possibly a superimposed dermatitis venenata.

A Case for Diagnosis (Melanosis of the Face and Neck; Keratosis Follicularis?). Presented by DR. BERANRD APPEL, Lynn, Mass.

C. S., a 28 year old white woman who is a brusher in a leather tannery, presents lesions of the face and neck of six months' duration. In May 1944 she started work filling bottles with glue which was thinned with carbon tetrachloride. In August the onset was marked by itching and the appearance of "bumps" and discoloration of the skin of the face and neck. By October her illness forced her to cease work.

Examination reveals uniform, closely placed macules in profuse and masklike distribution over forehead, cheeks, rami and neck. Their dark pinkish brown color produces a "dirty," pigmented appearance of the skin.

The results of the hematologic examination showed: hemoglobin, 90 per cent; erythrocytes, 3,720,000; leukocytes, 6,100, and a normal differential count. With the exception of a greenish yellow reaction for sugar, the urinalysis was within normal limits. The Hinton reaction of the blood was negative. A biopsy specimen showed moderate acanthosis and a collection of pigment in the upper portion of the corium.

Treatment consisted of the oral administration of vitamin A and reduced iron.

DISCUSSION

DR. JOHN G. DOWNING: I saw a girl in my office about two months ago who had a similar eruption. She had the lesions on the face and light brown macules

around the waistline. She had nothing else. I took her into the Evans Memorial Hospital and studied her carefully. I thought at one time a pathologic condition was present in the liver, but nothing definite was found on which to base an etiologic factor. Biopsy was performed with the idea that the eruption might be an unusual type of lupus erythematosus of a pigmented nature which has been described. I though it might be an unusual type of lichen planus. It is not my conception of the melanosis of Riehl as I saw it in Europe. It is not my idea of keratosis follicularis. I can only suggest negative evidence rather than positive.

DR. FRANCIS M. THURMON: Except for the distribution of the pigmentation and the dirty brown appearance, the lesions on the face are suggestive of berlock dermatitis, which is due to the topical application of some photosensitizing substance. I believe in this instance, since this girl works as a brusher in a tannery, the dermatitis may have been caused by some substance with which she came in contact.

DR. JOHN G. DOWNING: I should like to agree with Dr. Thurmon. The girl whom I observed was a welder, and of course she was exposed to the arc light and a certain amount of ultraviolet rays. The eruption on the waist was entirely different from the eruption on the face.

DR. E. MYLES STANDISH: I asked the girl carefully about cosmetics and whether or not she used perfumes. She uses La Salle powder and rouge. The only contact she made in the factory was with glue and carbon tetrachloride. I thought the eruption looked like lichen planus. There was a definite shiny aspect to the flat-topped papules.

DR. BERNARD APPEL: I took the opportunity of looking up something about melanosis, and there are a picture and a description in the Corpus Iconum Morborum Cutaneorum of the Budapest Congress of 1935. The picture, no. 4,465, depicts melanosis of Riehl. In that particular picture the lesions have more of a follicular distribution than this girl presented today. In that respect it is different. In respect, however, to all the cases that are described in that Corpus Iconum, particularly as to the relation of distribution of the exposed areas—areas which are obviously subject to photosensitization—I consider that this case resembles it. This case also resembles those described in the Corpus Iconum with respect to the color of the macules. Riehl himself had an interesting explanation of eruptions of this type, namely, that they are essentially a reaction of skin sensitized by sunlight. Practically all occur in women, and at one time Riehl felt that a dysvitaminosis was the basis of the sensitization. A man by the name of Baroni had an ingenious explanation. He reported a large number of cases and felt that the eruptions were due to face powder. The aniline dye in the face powder has a ring nucleus similar to that in tar derivatives which acts as in the cases which Riehl described in sensitizing the skin to the sun. He thought that in these cases the lesions were due to chemical sensitization rather than to dysvitaminosis. Histologically, this pitcure fits in with the description given by Riehl. There are some acanthosis and edema of the prickle cell layer. Collections of large granules of pigments obviously in clusters are present in the upper part of the corium. The pigment of the basal cell layer is less than expected. I think this probably is a case of melanosis of Riehl. Now, as to the question of the occupation of a brusher, it conists of placing the skins which have been completely tanned, dyed and finished into a machine consisting of two large revolving brushes which are made the same as the rollers of a wringer, only the fibers touch the skin lightly. Usually there is a suction device or hood ventilation that draws off the dust, but, even so, there is considerable dust around the machines. I have seen a number of patients who have had various dermatoses who are operators of brushing machines, and I have never seen anything like this eruption in any one in a leather factory. I think it will turn out to be a result of her having been sensitized to some cosmetic and the nature of it is melanosis of Riehl.

A Case for Diagnosis (Parapsoriasis?). Presented by Dr. Alfred Hollander, Springfield, Mass.

M. W., a 51 year old white man, presents a generalized eruption of nine months' duration. The onset was marked by a lesion 3 cm. in diameter on the left side of the forehead, to which various ointments had been applied topically, including sulfanilamide for one day. The eruption gradually spread over the face and by October had extended over the whole body. At the time he was first seen, in December, a generalized dermatitis was present, in addition to the psoriasiform lesions. The acute dermatitis and the itching subsided with mild topical applications.

The eruption on the face, arms and thighs is retiform in character. Reddish yellow plaques with fine scales are seen on the neck, forearms, trunk and legs. Guttate lesions also are present on the trunk. Removal of the scales by scratching reveals punctate bleeding points.

Histologic examination showed parakeratosis, acanthosis and infiltration in the upper portion of the corium.

Treatment consisted of Aquaphor (an oxycholesterol-petrolatum ointment), with 2 per cent salicylic acid topically and solution of potassium arsenite, U. S. P. internally.

DISCUSSION

Dr. George E. Morris: I believe this man has psoriasis rather than parapsoriasis. He has lesions on the penis, back and buttocks which are typical of psoriasis.

Dr. Walter F. Lever: I agree with Dr. Morris.

Dr. Jacob H. Swartz: I think it is psoriasis, but I should like to add the fact that one should consider premycosis fungoides with mycosis fungoides later.

Dr. Alfred Hollander: I have to admit that the histologic picture looks like psoriasis, but there are a few cases of parapsoriasis which show a picture which cannot be distinguished from psoriasis. When I saw the specimen, I considered the question of premycosis fungoides but in making a diagnosis I believe one has to consider the results of the treatment. This man has not had any antipsoriatic treatment. On the contrary, before I saw him, he was treated with many types of preparations, including ammoniated mercury, and he reacted with a generalized dermatitis. After that the lesions appeared again, as they are today, In my experience, parapsoriasis does not react at all to mercury or show a severe flare-up. Despite the rather typical histologic picture of psoriasis, I think this is parapsoriasis.

A Case for Diagnosis (Pseudopelade; Alopecia Cicatrista?). Presented by Dr. Bernard Appel, Lynn, Mass.

J. McL., a white school boy aged 12, presents lesions of three years' duration involving the scalp and the posterior portion of the neck. The onset was marked by a lesion which developed on the posterior portion of the neck following chickenpox. The eruption has varied in intensity but at no time has there been complete remission.

Examination reveals an area of atrophic scarring 4 cm. in diameter on the vertex of the scalp, the center portion of which presents a few hairs, while at the periphery there are areas of distinct folliculitis. On the occiput two lesions, each 3 cm. in diameter, showed active follicular inflammation with closely packed crusted papules and pustules. There is generalized dryness of the skin, particularly on the face, where it is tight and erythematous. Keratosis pilaris is generalized.

The results of hematologic examination showed: hemoglobin, 85 per cent; erythrocytes, 4,030,000, and leukocytes, 10,900, with a differential count of 68 per cent polymorphonuclears, 4 per cent eosinophils, 3 per cent monocytes, 1 per cent basophils, 22 per cent lymphocytes and 2 per cent large lymphocytes.

Cultures for fungi showed no growth, and there was no fluorescence of the hairs on illumination with the Wood filter.

No improvement was noted after the use of pine tar and sulfanilamide ointments.

DISCUSSION

DR. G. MARSHALL CRAWFORD: I suggest the diagnosis of folliculitis decalvans, assuming that favus has been ruled out.

DR. WALTER F. LEVER: I should like to add the diagnosis of lichen spinulosus.

DR. ALFRED HOLLANDER: I believe this is a typical case of folliculitis decalvans.

DR. JOHN G. DOWNING: As I said to one of the men, I think that if one wants to see a picture of the follicular papules of folliculitis decalvans this is an excellent example of it. In a child of this age, I would not make a diagnosis of pseudopelade or folliculitis decalvans until I ruled out an infectious process. I want to rule out favus or some other type of fungous infection. I think one should go to extremes to exclude pseudopelade, which to my mind is extremely rare.

DR. EDWARD A. LAFRENIERE: I suppose that what I am going to say is going to start a great deal of discussion. There is a group of diseases of unknown cause, and they all present distinct clinical pictures but histologically they are almost alike, varying only in the severity of the pathologic process. Now, for instance, pseudopelade shows hardly anything clinically except an atrophy and a slight pink discoloration around the edge, but histologically there is an inflammatory process starting at the neck of the follicle and gradually spreading down to the hair follicle but there is no gross inflammation clinically. Folliculitis decalvans gives a distinct picture clinically and grossly; the inflammatory process is severer microscopically, involving the hair follicle and giving microscopic abscesses. Both will heal with scar tissue and with some sclerosis which is softer in pseudopelade and harder in folliculitis decalvans. There is another disease, perifolliculitis capitis abscedens et suffodiens, which causes an inflammatory process going deeply into the tissue. Then there is the same thing in folliculitis keloidalis, which gives an inflammatory process localized in the follicle with a keloidal ending. I wonder whether twenty years from now these diagnoses will not be changed entirely and based on what is found in the form of an infectious process. For instance, years ago bronchopneumonia and lobar pneumonia, lobular pneumonia and wandering pneumonia were diagnosed as clinical entities, but now a search is made for the type of organism or virus causing the disease. I wonder whether twenty years from now the same thing will not hold true for this group of cutaneous diseases.

DR. BERNARD APPEL: I want to thank all the members for this enlightening discussion. I was much intrigued by Dr. Lafreniere's discussion. Dr. Lever mentioned lichen spinulosus. I have here a report entitled "Folliculitis Decavans and Lichen Spinulosus; A Clinical Combination" by Francis Senear published in the Transactions of the Section on Dermatology and Syphilology of the American Medical Association of 1920 in which he says that a number of cases are reported with that well known combination of folliculitis decalvans and lichen spinulosus of the trunk. Although this boy did not show the clinical picture of lichen spinulosus, he nevertheless did have other changes in the skin which are obvious and which fit in with some sort of dyskeratosis that is consistent with the picture previously mentioned that is associated with vitamin A deficiency. Obviously there is some relationship between the hair follicles of the scalp and the follicles of the body. I fear this case is going to turn out to be a case of folliculitis decalvans or pseudopelade or perhaps a superficial case which contains some of the constituents of each of those two pictures.

DR. FRANCIS M. THURMON: I believe Senear called attention to the frequent association of lichen spinulosus with folliculitis decalvans and suggested that the toxins elaborated by the disorder of the scalp may be influential in causing lichen spinulosus. In pseudopelade of Brocq there are no pustules. The patient seen today showed pustules.

DR. JOHN G. DOWNING: I enjoyed Dr. Lafreniere's discussion. I do not think one should let it go at that. I think he has the right idea. One must remember that most of these diagnoses have survived twenty years. The reasons that dermatologists go into the intricate diagnosis of these cases are, first, to give the patient a prognosis and to know whether therapy is going to be of any value and, second, as regards therapy, to discover what is going to be used in these cases. I think, just looking at these cases, that one should always try to differentiate between this type of folliculitis decalvans, pseudopelade and lupus erythematosus. Cultures have to be made, and histologic sections have to be taken.

A Case for Diagnosis (Panniculitis, Nodular, Nonsuppurative?). Presented by DR. FRANCIS M. THURMON, Boston.

A. L., a 68 year old white American woman, has had painful suppurative nodular lesions of the legs for the past thirty-eight years. During her youth she was treated for pulmonary tuberculosis, which has been arrested. When she was 30, ulcers of the legs were noted, which appeared three months after an immunizing dose of diphtheria antitoxin. The onset of each lesion was marked by a pink macule 2 to 4 mm. in diameter which was superimposed on a tender nodule 2 mm. in diameter. The lesion gradually enlarged to form a painful bluish-discolored nodule 2 to 4 cm. in diameter which eventually broke down with a serosanguineous discharge. Healing was slow, and a depressed atrophic scar resulted. The entire clinical course has been afebrile. Arthritis deformans has been present.

Examination reveals a few varicosities and numerous depressed scars involving the entire surface of the legs, with greatest intensity over the lowest third of the legs. The roof of a single lesion is thin and on the verge of erupting; the lesions are dark red, fluctuant and painful. Five draining ulcers are present. The extremities and fingers are deformed with arthritis.

Broth cultures, blood agar plates, agar slants and stained smears failed to reveal organisms. Stained smears showed 14 to 200 leukocytes per oil immersion field. A guinea pig inoculation was negative for tubercle bacilli. The blood sedimentation rate was 41 mm. in one hour. Examination of the blood showed: hemoglobin, 85 per cent; erythrocytes, 4,500,000, and leukocytes, 8,800, with a differential count of 62 per cent polymorphonuclears, 33 per cent lymphocytes and 5 per cent mononuclears.

Rapid healing of the lesions followed incision, drainage and irrigation with an 8 per cent solution of glycerite of hydrogen peroxide. Iron sulfate, vitamin B complex and ascorbic acid have been administered orally.

DISCUSSION

DR. GEORGE E. MORRIS: Thirty-five years ago this woman had roentgen rays directed to her thyroid gland as treatment for a "toxic goiter." She knows she had something wrong with her thyroid gland. I should like to suggest that she has localized myxedema.

DR. EDWARD A. LAFRENIERE: Several years ago Dr. Lane and I saw a case of panniculitis. The biopsy specimen was not seen by a dermatopathologist. The patient had the subcutaneous nodules which developed into sterile abscesses. This lady was very thin and emaciated and had an arthritic process in the hands, feet and knees, and she appeared to have the picture of tuberculosis. I wonder whether panniculitis is not a degeneratitve process following a toxic disturbance which apparently may be the cause of arthritis and other metabolic disorders.

DR. LORETTA J. CUMMINS: In talking with this patient, I was told that when she was a girl she had tuberculosis. At least two or three different physicians have diagnosed active tuberculosis of the apexes of the lungs. Many of these lesions on the legs have suppurated, and vaccines have been made. I do not believe it can be called nonsuppurative panniculitis, with that history.

DR. C. GUY LANE: I strongly doubt the diagnosis of nonsuppurative panniculitis in this case. Another curious item to me is the localization in the legs. A group of cases were reportred several years ago, and as I remember the lesions involved the thighs and, I am not sure, in one or two instances the calves as well. I think the localization is striking. One wonders whether there is some other factor, perhaps a circulatory factor, perhaps a fat factor, in this particular case.

DR. JACOB H. SWARTZ: I should like to offer a diagnosis of dermatitis nodularis necrotica.

DR. FRANCIS M. THURMON: I thought from the appearance of these lesions that they were infectious but all efforts toward demonstrating this by cultures and smears were unsuccessful. I can conceive of the possibility of a vaccine being made in the past from a contaminant, but I made cultures on blood agar plates, and agar slants and cultures on Sabouraud's medium from three different lesions and they were all sterile. A stained smear of the secretion showed the leukocyte count to vary from 14 to 200 per high power field. There were no organisms, and an acid-fast stain was negative for tubercle bacilli. I could not help but feel that this was in some way associated with tuberculosis in view of the definite history of pulmonary involvement when she was younger. Since that time she has been under the care of good clinicians who assured her there was no evidence of active tuberculosis. A guinea pig was inoculated and the report was negative for tubercle bacilli. There is no history of ingestion of a bromide or an iodide. The character of the lesions rules out erythema nodosum. It seemed to me that the history of the case, with the lesions beginning as small macules 2 to 4 mm. in diameter and painful nodes lying beneath the macules, going on to suppuration in seven to fourteen days, the lesions occurring in groups and the pain being relieved as soon as the lesions were opened and drained, is suggestive of a liquefying nodular panniculitis of an afebrile type, such as was described by Bailey in 1937. This is not the febrile relapsing nonsuppurative panniculitis because throughout the entire course of the process the patient has been afebrile. As near as I could come to a diagnosis agreeing with the pathologic diagnosis was chronic nonsuppurative panniculitis.

A Case for Diagnosis (Psoriasis of the Palms and Soles; Syphilis?). Presented by DR. JOHN G. DOWNING, Boston.

P. Z., an unemployed Polish man aged 42, presents lesions of the palms, soles and anterior surfaces of the arms of approximately eighteen months' duration. In 1937 he presented lesions which were diagnosed as psoriasis, and during the same year was inadequately treated for primary seronegative syphilis. He lapsed treatment until June 1944, when a large calloused indurated pruritic but nonpainful lesion appeared on the left heel. Soon the rest of the sole became involved, and similar lesions developed on the right side. Scarring, itching and fissuring of the palms appeared.

Examination reveals thickening, hyperkeratosis and fissuring of the palms and soles, with the periphery sharply outlined by an erythematous induration.

The Hinton reaction of the blood was negative.

Various ointments have been applied, and, despite ten treatments with oxophenarsine hydrochloride, potassium iodide orally and low voltage roentgen rays locally, there has been increased intensity in the processes.

DISCUSSION

DR. WILLIAM P. BOARDMAN: There certainly have been plenty of psoriatic palms and soles which have not responded to treatment. However, I am wondering whether this is really psoriasis.

DR. FRANCIS M. THURMON: I did not think that the lesions on his elbows and patella were psoriasis. They were follicular and appeared irritated.

DR. JOHN G. DOWNING: When I first saw this man, his hands were in bad shape. They were desquamating, infiltrated and hyperkeratotic. When he was examined, lesions were found elsewhere. He had a past history of syphilis. He was given treatment, but the lesions did not respond. I should like to know what to do for him.

A Case for Diagnosis (Psoriasis; Lichen Planus; Erythroplasia of Queyrat?). Presented by DR. GEORGE E. MORRIS, Boston.

C. K., a 60 year old white man, has lesions of the glans penis and prepuce which have gradually intensified during the past six months.

Examination reveals asymptomatic glistening erythematous infiltrations varying in size from 0.5 to 2 cm. in diameter on the glans penis and prepuce. A small amount of brown crusting is present.

Histologic studies revealed chronic inflammation.

DISCUSSION

DR. C. GUY LANE: I do not think that the eruption is erythroplasia. This does not have the shine and shape or outline seen in other cases. I should feel this was psoriasis in spite of the fact that it is unusually located.

DR. FRANCIS M. THURMON: I thought that was typical psoriasis of the genitalia, and did not think it was erythroplasia of Queyrat, because it did not show that shine and glazed surface or the slight thickening that characterizes erythroplasia of Queyrat. To be lichen planus of a confluent type such as that particular lesion was, it would have to be a hypertrophic type of lichen planus associated with itching, and itching was not present. Clinically, it was typically psoriasis.

DR. JOSEPH GOODMAN: I would agree with Drs. Lane and Thurmon about the clinical appearance of this lesion, but the microscopic picture shows infiltrating plasma cells and causes me to believe that it is erythroplasia of Queyrat. My conception of erythroplasia of Queyrat is that it is a precancerous dermatitis.

DR. WALTER F. LEVER: One may call it that if one wants to preserve the term "precancerous." Erythroplasia, as well as Bowen's disease, was originally described as precancerous, but it seems to me preferable to refer to them as early cancers. The characteristic changes are in both diseases, epithelial dysplasia and dyskeratosis, which, I believe, are evidences of early intraepidermal epidermoid carcinoma.

DR. ALFRED HOLLANDER: Clinically this case does not appear to be one of erythroplasia of Queyrat. First, there is no shiny apearance, and, second, the lesion is not localized. In erythroplasia the lesion would not be so widespread around the penis. Histologically this picture is compatible with psoriasis.

DR. GEORGE E. MORRIS: Clinically it was psoriasis, but histologically I was not so sure. Dr. Thurmon and I recently saw a man who was treated for psoriasis of the penis which turned out to be an epithelioma. This lesion has some infiltration. I think the patient should be watched a little longer.

DR. JOHN G. DOWNING: My diagnosis is psoriasis.

A Case for Diagnosis (Dermatitis Medicamentosa?). Presented by DR. JOSEPH GOODMAN, Boston.

J. A., a 64 year old white man, presents lesions of approximately eight months' duration on the arms and legs.

At the onset, lesions appeared on each calf and slowly extended to involve the legs. At times these areas were 15 cm. in diameter and were minute vesicles, some of which changed to pustules with an erythematous base. These spread peripherally; a scalloped border developed, and central healing occurred. Vesicles and pustules which recurred within healed areas contained fluid consisting in

great part of necrotic epithelium. Within a few weeks a similar eruption appeared on the arms. Later several areas developed on the forehead and occiput. Over the past two months there has been simultaneous involution of some lesions, while others have appeared. The healed lesions show pigmentation but no scarring. There was no history of ingestion of drugs.

The results of repeated hematologic examinations and urinalyses have been within normal limits. Chemical examination of the blood showed nonprotein nitrogen 42 mg., calcium 9.2 mg. and phosphorus 3.8 mg. per hundred cubic centimeters. The Hinton reaction of the blood was negative. Two cultures of new lesions yielded no organisms. The histologic examination suggested a drug eruption, particularly of bromide origin.

Local treatment has comprised moist dressings of potassium permanganate, boric acid ointment and low voltage roentgen ray therapy. Sulfadiazine administered in high dosage for two weeks was without benefit.

DISCUSSION

DR. C. GUY LANE: I saw this case some time ago, and it presents an entirely different picture now than it did at that time. In spite of the patient's denials there is in my opinion a great probability of this being a drug eruption. I do not know whether any reason has been found why he should be taking drugs. Earlier, without the acute phase of the vesicles with the purplish red appearance, there were many more pigmented patches than there are today. There were larger pigmented areas on his arms and less of a mottled appearance. This new acute attack, coming on quickly within a couple of weeks, would emphasize the matter of some toxic or drug factor. I shall be interested to know whether Dr. Goodman has obtained any more of the history.

DR. FRANCIS M. THURMON: I happened to stand behind the curtain when this patient was talking to somebody else, and he seemed to me to be somewhat of a verbal exhibitionist and glad to show himself off and talk about his dermatitis. I would not be surprised if this proved to be a factitious condition precipitated by the ingestion of phenobarbital or phenolphthalein.

DR. LEONARD E. ANDERSON: I am in accord with Dr. Thurmon and should like to see how he gets along on fixed dressings for a while.

DR. G. MARSHALL CRAWFORD: Another possible factor is that the patient knows he will not be operated on for his hernia as long as he has this eruption.

DR. JOSEPH GOODMAN: I have questioned this patient repeatedly about ingestion of drugs, before and after he saw Dr. Lane. On no occasion could I uncover anything that was suspicious. He runs a tavern and works behind the bar, and says that he has taken an occasional drink of rye but no mixed drinks, no cocktails and no wines. I have been unable to reach any conclusion other than that he has an eruption caused by a drug, but I am unable to find any history to support it. As to his tendency toward exhibitionism, I have been attempting to get him to a meeting for six months. It was with reluctance that he came today. He does not seem inclined to want to show these lesions to any one.

A Case for Diagnosis (Sarcoid; Leprosy; Lupus Erythematosus?). Presented by MAJOR EARL A. GLICKLICH, Lovell General Hospital, Fort Devens, Mass.

V. B., a 26 year old white man, a commissioned officer in the Army, presents lesions of the face and left hand of eight months' duration. He had been in the service for four years, twenty-one months of which had been spent overseas in Hawaii. He first noticed circular erythematous lesions on the right malar region in June 1944. He received six treatments with bismuth subsalicylate; stomatitis developed, and the use of bismuth was discontinued. He then received eight doses of gold sodium thiosulfate, totaling 210 mg., with decided improvement. He left on detached service for five weeks, and on his return the original areas

recurred and grew larger. He stated that the area was practically anesthetic. In addition he gave a history of a similar lesion occurring on the knuckle of the left index finger, of two years' duration, and of a lesion that developed more recently on the left ring finger.

With the exception of the cutaneous involvement, the physical findings are within normal limits. There is an oval indurated macular erythematous patch of dermatitis in the right malar area which is scaling and shows follicular dilatation. No telangiectasis is present. Similar lesions, although less extensive, are present on the knuckle of the index finger of the right hand and the third finger of the left hand.

The results of the examinations of the blood and the urine, as well as those of roentgenographic examinations of the chest, hands and feet, were within normal limits. Histologic examination showed essentially a tuberculoid structure.

DISCUSSION

DR. E. MYLES STANDISH: I thought the diagnosis was sarcoid. That seemed to fit well the lesions as shown and also the biopsy.

DR. BERNARD APPEL: I felt clinically it was sarcoid, but as the question of leprosy had been raised I wonder why an intradermal injection of histamine phospate has not been given. This is a definite test which was well described by Pardo-Castello and is almost specific for macular forms of leprosy.

MAJOR EARL A. GLICKLICH: How shall this man be treated? He has already had a bismuth preparation.

DR. ALFRED HOLLANDER: I propose the use of chaulmoogra oil. You will remember that several months ago Dr. Cheever presented the case of a young boy who had a similar lesion on the forehead. I recommended to Dr. Cheever the use of chaulmoogra oil, and he told me later that the lesion had improved. I have had good results with injections of chaulmoogra oil in some cases of sarcoid.

DR. JOHN G. DOWNING: I suggest injections of diphtheria toxoid.

DR. FRANCESCO RONCHESE: If it is sarcoid, it may spontaneously disappear.

DR. ALFRED HOLLANDER: Regarding the diagnosis of leprosy, I believe leprous lesions will not appear in such a short time. A lesion of leprosy will not appear before five or six years after exposure.

A Case for Diagnosis (Sycosis Vulgaris and Folliculitis of the Scalp?).
Presented by DR. BERNARD APPEL, Lynn, Mass.

J. K., a 23 year old white man, presents lesions of the face, scalp and pubis of two years' duration.

Two years ago, while he was employed as a welder in the Navy Yard, minute pustules developed on the bearded area of the face and on the back of the neck at the hair line. The lesions were moist, but the inflammation was minimal. At this time treatment with Staphylococcus vaccine, ultraviolet rays and roentgen rays produced improvement. He then was inducted into the armed services, and while he was stationed in Texas an exacerbation of these lesions occurred, with additional involvement of the scalp. Penicillin and local therapy produced no improvement. He then received a medical discharge.

Examination reveals involvement of the bearded areas with numerous small yellowish pustules on an erythematous raised indurated base. Hairs penetrate many of these discrete papules. The pubic area is similarly involved. On the scalp there are nontender red nodular perifollicular infiltrations. Numerous areas of alopecia with minimal scarring are present on the vertex.

The results of the urinalysis were normal. The blood count showed. hemoglobin, 102 per cent (Sahli), and leukocytes, 7,200 with a differential count of

60 per cent polymorphonuclears, 36 per cent lymphocytes and 4 per cent mononuclears. The results of cultures have not yet been reported.

DISCUSSION

DR. EDWARD A. LAFRENIERE: This is a case which seems to emphasize the point which I tried to bring out a little while ago. This man's disease started with sycosis of the beard, which spread to the scalp, giving him folliculitis. Three days ago there was a small area of furfuraceous scaling on the chin which I suspect was a fungous infection, probably complicated with a secondary staphylococcic infection. I understand that in cases of sycosis vulgaris it is not common for scar tissue to develop, although it does happen, as it did in this case, spreading to the scalp and giving some areas of thin, atrophic skin, some areas of a nodular type of lesion and several areas which are almost abscessed. Then the patient has lesions on the face which are suggestive of the papules of acne; some are secondarily infected—all of which leads to the conclusion that most human beings inherit a certain type of skin which may have allergy or anergy and may be susceptible to certain types of infections. This in addition to a staphylococcic infection, as in this case—a different strain of Staphylococcus—will give a different type of manifestation—a different type of location and different types of end lesions.

DR. FRANCIS M. THURMON: I believe, since it is known how persistent this entity is, one would not be justified in giving him a five day course of penicillin therapy.

DR. CARL D. SAWYER: Long ago I had a patient with extensive sycosis vulgaris, and I gave him a course of fractional doses of roentgen rays which cleared it, but after three or four weeks it broke out again.

DR. GEORGE E. MORRIS: I have a similar patient who has been seen by several physicians. He has had twenty-five roentgen ray treatments. He has had a good course of treatment with penicillin and sulfonamide compounds. He heard somebody recommend sulfur ointment. He got it from a druggist, and within two weeks he was better than he had been with all the ointments that had been prescribed for him.

Lupus Vulgaris. Presented by DR. FRANCESCO RONCHESE, Providence, R. I.

J. S., a 28 year old white man, an American-Italian farm worker, presents a lesion of approximately eleven years' duration on the right side of the head and face. At the time he was first seen, in 1935, he presented a yellowish red nodular lesion on the right temple. (See figure.) This lesion was destroyed by desiccation and curettage, resulting in an apparently well healed scar. However, one year later new lesions appeared at the edge of this scar and have continued to extend peripherally.

The active lesions are scaling raised soft nodular areas, involving the right side of the forehead, eye and cheek, and recently the conjunctiva of the right eye has been affected. The central portion of the area shows scarring and atrophy, resulting in part at least from therapy.

The Hinton and Wassermann reactions of the blood have been negative repeatedly. The reaction to tuberculin was positive. A histologic examination confirmed the diagnosis of lupus vulgaris.

Treatment has comprised desiccation, curettage, plastic surgery, use of roentgen rays, radium and radon implants, application of an ointment containing pyrogallol in a concentration of 10 per cent, bismuth therapy, injection of oxophenarsine hydrochloride, a salt-free diet and injection of Eulykol (phenylethyl esters of a selected fraction of the acids of hydnocarpus oil prepared by Burroughs Wellcome & Co., Inc.) and starch. (Starch is recommended as beneficial in lupus vulgaris.

A saturated solution of corn starch in sterile saline solution is used.) An area on the right eyebrow was excised and grafted. The process has now involved the grafted area, together with the skin and the mucous membrane of the right eyelid.

Lesions of lupus vulgaris: *A*, in 1935; *B*, in 1939; *C*, in 1944.

DISCUSSION

DR. LEONARD E. ANDERSON: His pictures show that nothing has been accomplished so far. The small lesion which developed in 1935 has become

extensive, and I think his only salvation is to find somebody bold enough to excise it.

DR. ALFRED HOLLANDER: I believe this is a typical case of lupus tumidus. In such cases the lesions have a tendency to develop into real keloids. I should be careful in going far into it because one may get rid of the lupus and new keloids will develop. I propose the Gerson-Hermannsdorfer diet for a therapeutic trial.

DR. FRANCIS M. THURMON: I think that no matter what is done for this man he will get worse.

DR. FRANCESCO RONCHESE: This case followed for eleven years offers a good example of what one may expect from treating an early lesion of lupus vulgaris otherwise than by wide surgical excision especially when the area, as in this case, is well suited for such a procedure.

This case was presented before the New England Dermatological Society on April 12, 1939 (Lupus Vulgaris [Tumidus], ARCH. DERMAT. & SYPH. **41**:427 [Feb.] 1940). As the "tumidus" variety of lupus vulgaris does, its clinical appearance resembled a nevus. Its unusual features are demonstrated by the discussion which followed. Its pathologic picture was that of tuberculosis of the skin, with acid-fast bacilli and with inoculation of the guinea pig being followed by development of tuberculosis. This patient has been followed since 1935, when the original lesion on his right temple (shown in the figure) was desiccated and curetted, resulting in a good scar and an apparent cure. The patient did not return as he was advised to do for observation. When he was seen again, six months later, a crop of new lesions had developed around the edges of the scar. The eruption has peripherally advanced ever since.

Surface application of radium, radon implantation and roentgen irradiation gave the best result, as clearing can be seen in the central area. However, these procedures failed to stop the peripheral advance. The injections of Eulykol and starch and the antisyphilitic therapy and the application of 10 per cent pyrogallol ointment had no effect whatsoever. A salt-free diet was prescribed, but as usual it cannot be followed properly if the patient is not hospitalized. An area on the right eyebrow was successfully excised and a graft applied. At present the disease has involved the grafted area and the skin and the mucous membrane of the right eyelid.

DR. FRANCIS M. THURMON: I saw a patient with lupus worse than this at the Atlantic Dermatological Conference in Washington ten years ago. His condition was a good example of what this disease will finally become.

NOTE.—From January 1946 to August 28 the patient received calcium gluconate, 10 cc., intragluteally, three times a week and 2.5 mg. of crystalline vitamin D_2 (Drisdol, Winthrop Chemical Company, Inc.), daily, by mouth, according to the method suggested by Charpy (*Bull. Soc. franç. de dermat et syph.*, November-December, 1943, p. 340). No ill effect from the medication has been noticed. The calcium content of the blood varied from 10 to 10.5 mg. per hundred cubic centimeters. The result has been most gratifying. The tumid lesions have flattened down completely to brown hyperpigmented areas. No new peripheral lesions have appeared. There is no more discomfort. The lesions appear to be healing completely.

In the last few months other patients having lupus vulgaris were treated in the same way, with encouraging results.

CHICAGO DERMATOLOGICAL SOCIETY

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Feb. 21, 1945

A Case for Diagnosis (Cutaneous Leishmaniasis?). Presented by DR. E. M. SMITH JR.

T. T., a white woman aged 43, complains of multiple chronic ulcers of the skin. While in Florida in March 1937 she noticed a tiny hole in the skin, with a slight discharge. Several more of these sinuses appeared but never with an acute inflammatory reaction. In June her physician cauterized the area with actual cautery, but the discharging sinus persisted and a new one appeared 2 inches (5 cm.) from the original one. Repeated attempts at excision of the area have resulted only in a spread of the process. The patient was seen in the clinic of St. Luke's Hospital in February 1938, at which time she had several large ulcers on the back, which did not seem deep and had little inflammatory reaction around them. The skin was undermined for a distance of about half an inch (1 cm.). Various dressings made little improvement. The ulcerated lesions on the back healed after thirty-six injections of stibophen (Fuadin), the last injection being given in April 1939. In August 1944 the patient returned with a similar ulcer over the area of the right biceps muscle. This lesion had been present for five years. During the interval she had been without treatment and without improvement, according to her statement.

An intramuscular injection of a small dose of the antimony preparation resulted in collapse of the patient. In October 1944 she noticed a tender nodule appearing in the subcutaneous tissues over the area of the left deltoid muscle. This lesion had a tendency to come to the surface and has been removed for histologic examination. At the present time there is another nodule in the same area.

Two inoculations of a guinea pig with material from the ulcer produced no pathologic changes. A roentgenogram of the chest showed no recent pathologic changes; "there is some old thickening in both lower lobes especially the right, with probably some bronchiectasis." A recent smear showed no acid-fast bacilli. Gram stains showed many leukocytes and erythrocytes but no organisms. Aerobic and anaerobic cultures showed no growth in seventy-two hours. Sodium hydroxide preparation showed no fungi or mycelial threads. No actinomycetes were found on the dextrose agar plate, but one culture showed a light count of Staphylococcus aureus. The dark field illumination did not reveal any trypanosomes or similar organisms. The Kahn and Wassermann tests were consistently negative.

A histologic section removed from the subcutaneous nodule showed noncircumscribed areas of focal necrosis deep in the stratum corium and extending into the fat layers, such as might suggest embolic foci of necrosis, and chronic granulation of subcutaneous fat tissue such as might be found in a case of embolic tuberculosis. No Leishmania bodies were identified.

DISCUSSION

There was no discussion of this case.

Iododerma with Secondary Streptococcic Infection. Presented by DR. FRANCIS E. SENEAR, DR. MARCUS R. CARO and (by invitation) DR. C. H. STUBENRAUCH JR.

F. H., a white woman aged 36, was seen for the first time at the University of Illinois in December 1944, at which time she presented a palm-sized ulcerated, vegetating and scarred area on the extensor surface of the left forearm. This lesion had been present for eight months. During this time it had become worse on two occasions, after the administration of sulfonamide compounds and after the

start of a course of injections of sodium iodide. One week before this first visit several new abscesses had appeared on the left forearm and the right leg. The patient had been taking a tonic containing potassium iodide for several days previous to the development of these new lesions. She stated that she had taken no medicament previous to the onset of the original lesion but admitted using iodized salt freely.

At the time of the patient's first visit to the clinic a pure culture of hemolytic streptococcus was obtained from each of several unruptured abscesses. The patient was given 1,200,000 units of penicillin intramuscularly in the course of about two weeks, with resultant healing of all abscesses and improvement in the vegetating lesions on the left forearm and the right leg.

The patient returned to the outpatient department yesterday and stated that the present lesions had become active when she received sulfathiazole after a miscarriage a few days ago.

The histologic examination of a section removed from the lesion of the forearm showed suppuration and the presence of many cocci.

DISCUSSION

DR. FRANCIS E. SENEAR: The interesting thing in this case, in addition to the findings which were presented and also brought up in the history, was that the patient had a dermatitis as a result of her ingestion of one of the sulfonamide compounds while in the hospital for treatment of this iododerma complicated with streptococcic infection. She made a complete recovery and was discharged. Then some one gave her one of the sulfonamide compounds, and she had a recurrence in the original site of the iododerma. I have seen 1 or 2 instances in which there was a focal reaction following ingestion of a sulfonamide compound in a patient who had a dermatitis due to some other agent. I wonder if any one else has made any observations in similar cases.

A Case for Diagnosis (Purpura Annularis Telangiectodes?). Presented by DR. FRANCIS E. SENEAR and DR. MARCUS R. CARO.

F. A. J., a white woman aged 53, first noticed a small red patch above the right cubital fossa about two and a half years ago. When she first came under our observation, on Aug. 8, 1944, there were several lesions on the flexor surface about the right elbow. Several other lesions have appeared since then, and these have gradually increased in size.

At the present time there are several poorly outlined patches, from the size of a pea to that of a dime, above and below the right cubital fossa. They are slightly erythematous, the erythema being almost entirely expressible. There is slight atrophy in the lesions, and small purpuric macules and telangiectases are present. There are no symptoms.

The urine was normal. The Wassermann and Kahn tests of the blood were negative. An examination of the blood showed 4,200,000 erythrocytes and 8,600 leukocytes, with a differential count of 44 per cent lymphocytes and 56 per cent neutrophils. The hemoglobin content was 85 per cent.

A histologic section taken from a lesion showed the epidermis to be flattened, with intracellular edema of the basal layer. Some of the superficial blood vessels were greatly dilated, while others were surrounded by circumscribed mantles of densely packed infiltrating cells, largely lymphocytes. Weigert's stain showed the elastic fibers to be destroyed in the areas of infiltration.

DISCUSSION

DR. L. H. WINER, Minneapolis: The microscopic section shows much more than one would be led to think was present from the clinical picture. Cells of many types participate in the infiltration, but the preponderant cells appear to be those that tend to form capillaries. There are also dilated capillaries in the section.

This infiltration is rather extensive, and, as a result of the microscopic appearance, I should favor a diagnosis of angioma serpiginosum of Hutchinson.

Dr. M. J. Reuter, Milwaukee: I was nonplussed when I observed the patient. I did not see the histologic section. I considered the diagnosis mentioned by Dr. Winer (angioma serpiginosum of Hutchinson), but I thought that the diagnosis was probably purpura annularis telangiectodes because I believed that there was definite purpura present.

Dr. Marcus R. Caro: When the patient first came in to see us, the lesions were so insignificant that I wondered why she bothered about them. They seemed to be patches of slight dermatitis that should have responded to simple medication like the application of zinc oxide ointment. In spite of treatment, however, they continued to enlarge, and biopsy was performed. We were surprised to see the amount of pathologic change, which was greatly out of proportion to the clinical appearance. I do not believe that the pathologic observations fit in with the diagnosis of purpura annularis telangiectodes or angioma serpiginosum, but I cannot make a definite diagnosis.

Parapsoriasis Guttata (Pityriasis Lichenoides Chronica). Presented by Dr. Stephen Rothman and Dr. H. Krysa (by invitation).

A. S., a white girl aged 16, was first seen in the University of Chicago clinics on Jan. 19, 1945. She presented a widespread papulosquamous eruption of ten to twelve days' duration, which was slightly pruritic. She gave a history of getting a vesicular eruption whenever she took cod liver oil or goose fat. She also had had "psoriatic spots" at the age of 6 or 7 years. Four years ago she was ordered to take thyroid because of obesity, and since that time she has been taking this drug with short interruptions. The basal metabolic rate has varied from —16 to —20 per cent. When she was first seen, she was taking iron, calcium and vitamins in irregular doses at irregular intervals. Twelve days prior to the appearance of the eruption, the patient had a sore throat and took sulfathiazole, 4 Gm. the first day and less on the second day. Ten days later the eruption appeared, first on the front of the neck and on the hands and the arms, and then spread rapidly to become generalized.

The eruption consists of discrete, sharply circumscribed, scaling erythematous lesions, 2 and 3 mm. in diameter. The scale on some lesions can be removed like a collodion membrane. There is no bleeding phenomenon.

The urine was entirely normal. The Kahn test was negative. The blood showed: hemoglobin, 14.3 Gm.; erythrocytes, 4,360,000; leukocytes, 7,700, with a differential count of 62 per cent neutrophils, 26 per cent lymphocytes, 9 per cent monocytes and 3 per cent eosinophils. The basal metabolic rate was + 12 per cent. A fluoroscopic examination of the chest showed no pathologic changes.

A histologic section taken from a lesion showed parakeratotic scales and a chronic inflammatory perivascular papillary and subpapillary infiltrate.

Ultraviolet irradiations and applications of ammoniated mercury ointments have been ineffective up to the present time.

DISCUSSION

Dr. H. E. Michelson, Minneapolis: Often I see a patient for whom the diagnosis rests between psoriasis and parapsoriasis, and usually when there is much question I find that eventually the disease turns out to be psoriasis. In this particular case there is not much in the microscopic picture that points to psoriasis.

Dr. Maurice Oppenheim (by invitation): The differential diagnosis between psoriasis and pityriasis lichenoides chronica is difficult in the case presented today. The form of scaling speaks more for psoriasis despite the absence of bleeding. The color and the location are more common in psoriasis. I did not see the histologic section, but I think that the disease is a superficial form of psoriasis.

DR. S. W. BECKER: The histologic section is not typical for psoriasis, but the mother stated that the child had had a psoriasis-like eruption at the age of 6 or 7 years. It would seem to be in favor of a diagnosis of psoriasis rather than parapsoriasis because the eruption disappeared entirely and recurred only recently.

DR. FREDERICK R. SCHMIDT: Simply stroking the skin will produce redness due to increased vasolability. It is present in most cases of parapsoriasis. That phenomenon is absent in this case.

DR. FRANCIS E. SENEAR: I should like to add one more piece of evidence in favor of psoriasis. I scraped a good many of those lesions but could not find anything except a minimal amount of scaling, not the powder-like scaling seen in parapsoriasis after guttage.

A Case for Diagnosis (Fat Necrosis?). Presented by DR. L. F. WEBER and DR. IRENE NEUHAUSER.

F. W., a woman aged 38, four months ago had an acute exacerbation of undulant fever following an infection of the upper part of the respiratory tract. The cutaneous and agglutination tests revealed the presence of undulant fever at that time. Since Nov. 6, 1944 the patient has received twenty injections of undulant fever vaccine at the rate of two a week. The vaccines of both Parke, Davis & Company and Lederle Laboratories, Inc., were used. A severe systemic reaction accompanied each injection. Severe local reactions also occurred, not only in the area in which the vaccine was given but at the sites of previous injections. The site of the original cutaneous test, which was indurated and inflamed, would also flare up and drain.

Examination reveals many superficial and deep firm nodules varying in size from that of a pea to that of a hickory nut on the extensor surfaces of both arms. On the extensor surface of the right arm and on the left thigh are bean-sized fluctuating areas. On the right thigh there is a similar lesion, which is draining. On the flexor surface of the left forearm is an erythematous, indurated, scarred area, which is practically crust covered.

A nodule over the region of the right triceps muscle was removed for histologic study, and the surgeon reported that macroscopically it appeared to be an area of fat necrosis surrounded by a cyst wall. This material when cultured yielded no organisms. The fluctuating area in the same region was aspirated several times and a clear fluid obtained, which appeared to be a liquid fat.

The histologic examination of a section from the nodule showed that it consisted of an inflammatory cyst; the cyst wall was composed of a chronic granuloma with considerable fibrosis. Many of the cells were foam cells, but staining for lipoid substances could not be done because the specimen had been prepared in alcohol.

DISCUSSION

DR. MARCUS R. CARO: About ten years ago Dr. Wien and I reported 3 cases of traumatic epithelial cysts of the skin (Traumatic Epithelial Cysts of the Skin, *J. A. M. A.* **102**:197 [Jan. 20] 1934). In 2, the lining membrane was composed of epidermis, while in the third case it was a layer of chronic granuloma and fibrosis similar to that seen in the present case. Unfortunately the fat stain could not be obtained in this specimen, but a number of foam cells were present, suggesting that fat was present. About a year ago Dr. Cornbleet presented before this society a girl with a number of ulcers on the skin at the site of injection of protamine zinc insulin. Histologically these also showed cystic granuloma formation. In the present case one may be dealing with fat necrosis or a foreign body reaction.

DR. PAUL O'LEARY, Rochester, Minn.: Lesions of this type are occasionally seen following injections of insulin, pituitrin and an extract of adrenal cortex. I do not believe that a toxic product in the preparation is the cause of the necrosis because I have observed 2 patients who received injections from the same ampule,

1 of whom had a large nodule which became necrotic while the other patient had none. The former patient had been having similar reactions from previous injections. I have accordingly been impressed with the possibility that reactions of the type displayed by the patient presented are the result of an immunologic or an allergic state of the patient rather than the result of administration of an impure product.

DR. IRENE NEUHAUSER: Apparently this type of reaction is not uncommon with undulant fever. Usually this reaction does not occur with the abortus strain but does occur with the melitensis and suis strains of Brucella. Since investigators have found that the abortus strain is just as effective when used therapeutically, it might be better to use this strain.

Acanthosis Nigricans Juvenilis? Presented by DR. I. M. FELSHER and DR. E. P. LIEBERTHAL.

C. K., a white girl aged 15, was admitted to the dermatologic department of the Mandel Clinic of Michael Reese Hospital on Dec. 5, 1944. At that time she presented subcutaneous lesions in the supraclavicular areas, on the sides of the neck and in the axillas, characterized by dark brown pigmentation and numerous soft, reddish brown papules or verrucous growths, varying from 1 to 3 mm. in diameter and of more than two years' duration. The pigmentation was lighter at the periphery of these areas. There was no complaint of any subjective symptoms. The patient was somewhat retarded mentally. Her father had active pulmonary tuberculosis about ten years ago. The disease is now in an arrested state.

At the present time the results of a physical examination and laboratory studies, including a complete blood count, a urinalysis, a chemical examination of the blood, an examination of the stool, a determination of the basal metabolic rate and a study of roentgenograms of the chest, are all within normal limits. Serologic tests for syphilis gave negative results.

A histologic section taken from a lesion of the left supraclavicular area revealed acanthosis, hyperkeratosis and hypertrophy of the granular layers in parts, with a definite increase of pigment in the lower rows of the rete and the basal layer. There were also numerous chromatophores loaded with pigment in the papillae and the subpapillary layer of the corium. The blood vessels were surrounded by a chronic inflammatory infiltrate and chromatophores that had some granular pigment.

DISCUSSION

DR. CLARK W. FINNERUD: I did not see the sections, but I thought that the eruption was Darier's disease, judging from the lesions of the neck, but the lesions of the lateral surface of the arms I thought were keratosis pilaris. I think that this would be an excellent case, from the standpoint of both of these disorders, in which to try out on intensive therapy with vitamin A.

DR. CARL W. LAYMON, Minneapolis: I agree with Dr. Finnerud that the case is one of keratosis follicularis. The lesions on the hard palate are consistent with such a diagnosis.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I agree with Dr. Finnerud. The girl is said to have mental retardation as well.

DR. PAUL O'LEARY, Rochester, Minn.: This patient presented another feature of Darier's disease, namely, the tendency to become moderately improved or to become greatly improved during the winter, only to have the keratotic lesions recur during the summer months.

DR. I. M. FELSHER: When we first saw the patient in December, the picture presented was entirely different from what it is today. The patient had diffuse pigmentation that was dark, in those areas, and verrucous lesions about five or six times the present size. We considered immediately the possibility of Darier's disease. However, I labeled this presentation "acanthosis" for the sole purpose of provoking a discussion, particularly on the possibility of obtaining beneficial

effects with vitamin A in instances of acanthosis nigricans juvenilis. This patient has received 100,000 units of vitamin A daily in the last three months, and she has made noteworthy improvement. At present there is little pigmentation left, and the verrucous lesions have cleared to about one fifth of their former size. The histologic section showed sufficient dyskeratosis to be compatible with keratosis follicularis, but the hyperkeratosis and increased pigmentation could also include the possibility of acanthosis nigricans juvenilis.

Epidermolysis Bullosa (Acquisita). Presented by DR. EDWARD A. OLIVER and (by invitation) DR. A. GREENBERG.

B. R., a man aged 32, suffered repeated attacks of a bullous type of eruption on the hands, brought on by any type of trauma, of two years' duration. These lesions ruptured and occasionally became infected. The same process occurred on his neck, probably due to collar irritation. No other areas have been involved. The patient has undertaken careful family research but has found no similar or related disease.

A physical examination two weeks ago showed some small bullous eruptions on the dorsal outer aspect of both hands. These lesions contained a clear, watery serum, which was sterile on culture.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: In the acquired type of epidermolysis bullosa, especially when bullous lesions appear on the exposed surfaces of the skin, it may be well to look for a possible disturbance of porphyrin metabolism. Sometimes there are melanosis and hypertrichosis as well and also vague abdominal symptoms and an indeterminate decline in general health, particularly an unexplained loss of weight. In one such patient in my experience recently, a woman in her fifties, such a train of symptoms was explained on this basis. There were large amounts of uroporphyrin in the darkened urine and also some indication of impaired hepatic function. With regard to my patient's sister, porphyrinogens were demonstrated in the urine, although she was in perfect health. This indicates that such a disturbance of metabolism may be familial and perhaps may remain dormant throughout life.

Generalized Erythroderma with Lipomelanotic Reticulosis (Pautrier and Woringer). Presented by DR. EDWARD A. OLIVER and (by invitation) DR. A. GREENBERG.

J. L., a Negro man aged 33, contracted bilateral inguinal adenopathy while he was stationed in the southern part of England in January 1943. This was followed by spreading, extensive scaling and pruritus of the skin. There is no family history of ichthyosis or memory of a previous similar episode in childhood.

Physical examination reveals scaly lichenification of the upper extremities, the hands, the abdomen and the lower extremities. There is generalized adenopathy, with the inguinal region being most involved.

The serologic study showed no evidence of syphilis, and the blood counts were within normal limits.

A histologic section from one of the lesions is presented.

DISCUSSION

DR. S. W. BECKER: I think that when a severe dermatitis develops in a patient he does a lot of scratching, and the glandular enlargement in this case may be due chiefly to secondary infection. Evidently considerable pigment is absorbed from the deeply pigmented epidermis and is deposited in the lymph nodes. I think that this patient has pronounced lymphadenopathy, with melanosis of the lymph nodes secondarily.

DR. RUBEN NOMLAND, Iowa City: After reading the original article on this disease I became interested and made several histologic sections of lymph nodes of

patients who had generalized exfoliating dermatitis and enlargement of the lymph nodes. Both lipoid substances and pigment were present in the lymph nodes, but the general pathologists did not think this unusual. They said that melanin pigment and probably lipoid material are found at most autopsies in which they examine the lymph nodes. They thought that it was nothing but a phagocytosis of foreign material derived from the skin and elsewhere. It is probably more pronounced in exfoliative dermatitis because of the inflammatory condition of the skin.

Mycosis Fungoides. Presented by DR. OLIVER S. ORMSBY.

R. E., a man, has had the present disorder for five and a half years. The eruption began on the right flank and gradually spread over the entire body. When the patient was first seen by me two and a half years ago, there was a diffuse eruption involving the neck, the trunk, the front, the arms, the forearms, the thighs and the legs. The lesions consisted of crescentic, round and oval plaques, moderately elevated and varying in size from that of a small coin to that of a palm. Numerous plaques had depressed centers and elevated margins.

The patient has had roentgen ray therapy almost constantly for three years. A large number of the plaques have cleared, but new ones have developed. The eruption has been associated with much itching. Asiatic pills (a preparation of arsenic trioxide and black pepper) given for the last three years together with the roentgen ray therapy have kept the disease under control.

About three years ago a histologic study of a section taken from one of the lesions confirmed the clinical diagnosis of mycosis fungoides.

DISCUSSION

DR. PAUL O'LEARY, Rochester, Minn.: I believe that chaulmoogra oil and fever therapy make the patient with mycosis fungoides more comfortable and occasionally slow up the progress of the disease. Perhaps this observation is due to the fact that the patients treated in this manner had a mild form of the disease and were destined for a long, protracted course. Nevertheless, the pruritus has been definitely decreased. A number of patients thus treated eventually presented exfoliative reactions and bizarre features of the disease that clinically were not typical of mycosis fungoides. In several cases in which roentgen ray therapy had been given to the point where the plaques did not melt out after its further use and after a course of chaulmoogra oil and hyperthermy, the plaques faded out after further treatment with roentgen rays.

DR. OLIVER S. ORMSBY: I presented this patient on account of the fact that he has had this disease for five and a half years. It has been extensive. It was treated with roentgen rays locally and with arsenic internally. I think that this treatment has held the disease in abeyance. A patient who has been so severely affected as this patient has been would usually have had serious results in five and a half years.

Calcinosis in a Burn Scar. Presented by DR. EARLE R. PACE.

J. O., a man aged 37, suffered a severe burn of the right pectoral region at the age of 7 years. The resulting scar was soft and supple except for an irregular firm area at about the site of the missing right nipple. About six or eight months ago this keloidal tissue was torn open while the patient was lifting heavy crates. A physician prescribed a cod liver oil ointment, which has been used continuously since that time.

When seen two weeks ago this patient presented a roughly triangular granulomatous lesion with a rolled, friable border, which was elevated about 3 mm. This was continuous around what appeared to be a central hard black blood "crust." Attempts to remove the "crust" led to profuse bleeding. The initial impression was that of an epithelioma with a peculiarly tough blood crust. Histologic examination of a section taken from the upper rolled border showed granulation tissue, with no evidence of malignancy.

Subsequent efforts to remove the "crust" revealed it to be bony-hard and evidently calcareous. Chunks were cut away with a heavy bone snip. After the decalcifying procedure these fragments showed no cellular structure.

In addition to this spike, which originally measured about 25 by 10 mm., there are two small circular deposits above the principal lesion which have bared their surface during the past two weeks. Much of the large spike has been cut away. Roentgenograms suggested that the calcinosis was relatively superficial. There is now present a palpable subcutaneous hard cord extending upward about 4 cm. from the ulcer. Surgical excision of the area and grafting are contemplated, and suggestions are invited.

The histologic section from the ulcerated area showed the histologic changes of a chronic granuloma containing considerable iron pigment. The other specimens were completely calcified.

DISCUSSION

DR. EARLE R. PACE: There was much more to the picture about two weeks ago. It was a granulomatous mass with a huge blood clot in the center. At the time I took the histologic section it was friable. I do not know whether the members palpated the lesion, but there was a core of calcium in the center plus extensions upward under the skin. I would be interested to know if any one has an idea of how to get rid of that core.

Symmetric Melanosis (of Genetic Origin?). Presented by DR. STEPHEN ROTHMAN and DR. H. KRYSA (by invitation).

R. P., a Negro man aged 37, had been in perfectly good health and had never had any disease of the skin until 1930 when he noticed freckle-like spots on both cheeks, which grew until they occupied almost the entirety of both cheeks. In the past five or six years his eyebrows have become thinner, and patches of hyperpigmentation have appeared on the skin of the supraorbital ridges. Recently he noticed similar spots in front of his ears. No itching or reddening preceded the appearance of these spots. An aunt who died many years ago was said to have had a similar hyperpigmentation.

Physical examination reveals strictly symmetric patches of hyperpigmentation of a dark brown shade on both cheeks. The skin is smooth, oily and apparently of normal texture and contains a normal amount of hair follicles. There are also two symmetric horizontal patches parallel to, above and below, the outer seven eighths of both eyebrows. The left of these meets the left patch of the cheek. The outer parts of the eyebrows are sparse and short.

Histologic sections taken from the preauricular area showed an atrophic epidermis and dilated follicular pores but no signs of lupus erythematosus. Histologic sections treated according to Becker's dopa method showed moderate dopa activity. Silver stain showed hyperpigmentation.

DISCUSSION

DR. S. W. BECKER: I talked to this man briefly, and I think that he has typical chloasma, which is not uncommon. I do not know how frequently it occurs in families. Both histologically and clinically it is chloasma.

DR. MAURICE OPPENHEIM (by invitation): The disease reminds me of melanosis caused by essential oils like oil of bergamot, by lubricants and by tar products.

DR. S. W. BECKER: The histologic sections showed that the melanosis was limited to the epidermis, which is different from the picture shown in melanosis due to sensitization. In the latter condition there is a lot of melanin in the chromatophores, and the color is grayer.

Subacute Disseminated Lupus Erythematosus. Presented by Dr. Stephen Rothman and Dr. H. Krysa (by invitation).

S. K., a woman aged 36, was first seen in the University of Chicago clinics on Sept. 29, 1944. She presented the typical picture of chronic discoid lupus erythematosus, with lesions on the scalp and both ears and above the right upper lip. The patient stated that she first noticed patches of alopecia of the scalp five years ago and that since that time these have spread steadily and progressively. Otherwise the personal and the family history were noncontributory.

The urine was normal. The serologic tests were negative. The blood count showed 5,000 leukocytes, 3,950,000 erythrocytes and a hemoglobin content of 12.4 Gm. Chemical examination of the blood revealed nonprotein nitrogen 19 mg. and total serum protein 7.7 mg. per hundred cubic centimeters and an albumin-globulin ratio of 4.89:2.81, equaling 1.74.

Histologic sectioning of the cutaneous lesions was not permitted.

The patient was given a course of weekly intravenous injections of ammonium succinimidoaurate. She received 25 mg. on September 29, 50 mg. on October 5, 75 mg. on November 1 and 100 mg. on November 10. The leukocyte count and the urine were checked during this course several times and were found to be normal. On November 15, five days after the last injection, the patient presented herself with an erythematous and papular eruption occurring on the dorsa of the hands, the palms, the forearms and the soles in the fashion of a toxic eruption. There was intense itching but no systemic sign or symptom; particularly, there was no stomatitis, enteritis or renal damage. The leukocyte count was 5,600. Sodium thiosulfate was ordered, to be taken intravenously and orally.

Since November 1944 the eruption has slowly improved, but it is still persisting. It now consists of reddish to violaceous macules, some of them displaying adherent scales, partly diffused over the macule, partly held in follicular plugs. The patient has again refused to have histologic sections taken.

DISCUSSION

Dr. Louis A. Brunsting, Rochester, Minn.: The patient presents discoid lupus erythematosus of the face, and the widespread lesions elsewhere, which are also discoid in character, represent a generalization of the process. The prognosis in such instances usually is milder than that in cases of subacute disseminated lupus erythematosus.

Dr. Francis E. Senear: Dr. Brunsting's remarks made me recall a comment made by Dr. Hamilton Montgomery several years ago. At that time I presented a patient showing disseminated lesions of lupus erythematosus, these lesions being of the discoid type but somewhat more acutely inflammatory than those observed in the usual case of chronic lupus erythematosus. That patient was definitely ill. She had lost weight, suffered from a moderate degree of prostration and showed mild leukopenia. At that time Dr. Finnerud questioned the diagnosis of subacute disseminated lupus erythematosus on the ground that the patient did not present an erythematous type of dermatitis. In reply to this Dr. Montgomery stated that at the Mayo Clinic they used the term "disseminated lupus erythematosus" with respect to the degree of systemic involvement which the patient showed rather than with reference to the cutaneous picture. He stated that in patients who presented systemic manifestations of the degree usually encountered in the subacute disseminated type that designation would be used even though the patient presented lesions which were essentially of the discoid rather than of the erythematous type. He also stated that it was the experience of the Mayo Clinic that about 50 per cent of the patients showing systemic involvement of a subacute degree usually succumbed.

I saw the patient to whom I have just referred at school yesterday for the first time in a year or so. She is still an extremely sick person, and I have no doubt but that she will die of her lupus erythematosus, although the eruption is still of the localized discoid type.

DR. PAUL O'LEARY, Rochester, Minn.: I use the following classification for lupus erythematosus: chronic discoid, localized, generalized; subacute disseminated; acute disseminated; special types, such as bullous and Libman-Sacks syndrome type. The classification is made not only on the clinical features but on the degree of the systemic manifestations as well. Leukopenia and an increased sedimentation rate indicate the degree of systemic involvement, and as the leukopenia becomes greater and the sedimentation rate higher the degree of toxemia is likewise increased. Disproportion in the serum protein-globulin ratios is a result of and not the cause of the systemic reaction. I believe that many of the patients with the subacute form of the disease have minimal cutaneous signs, frequently unrecognizable, although the associated arthralgias and the state of exhaustion may be severe enough to keep the patient confined to bed. A young woman who has arthralgia, fever and leukopenia should be suspected of having the subacute phase of lupus erythematosus, although the cutaneous signs alone do not permit such a diagnosis.

Lupus Erythematosus. Presented by DR. IRENE NEUHAUSER.

C. T., a woman aged 42, noticed red patches on the sides of her neck about five months ago. She thought that they were due to irritation from a starched collar, but the patches persisted and have progressed slightly. She is conscious of some sensitivity in this area, but there are no other subjective symptoms. No medication or cosmetics were applied to this area before or after the disease developed.

Examination reveals hyperpigmented atrophic patches of irregular configuration on each side of the neck, extending from the subauricular region to the clavicle. There are telangiectasia, some prominent follicles and a few scanty adherent scales in this area.

The urine was normal. The blood counts were: erythrocytes, 4,360,000, and leukocytes, 6,700, with a differential count of 61 per cent neutrophils, 22 per cent small lymphocytes, 6 per cent large lymphocytes, 8 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils. The hemoglobin content was 82 per cent.

A histologic section taken from the neck showed a thin non-nucleated scale and a flat atrophic epidermis with a continuous granular layer and liquefaction of the basal layer. In the upper part of the corium there was a densely packed infiltrate of lymphocytes, histiocytes and many chromatophores, which extended almost to the epidermis. Narrow mantles of the infiltrating cells extended a little more deeply about some of the blood vessels. The Weigert stain showed the elastic fibers to be thinned and fragmented in the infiltrated areas.

DISCUSSION

DR. FRANCIS W. LYNCH, St. Paul, Minn.: Since the lesions are not characteristic of lupus erythematosus, I am forced to disagree with that diagnosis, although I have no definite diagnosis to offer in its place. The histologic section suggests that the patient might have lichen planus, but the eruption has slight resemblance to that disease.

DR. LOUIS H. WINER, Minneapolis: I agree with Dr. Lynch that the histologic section suggests lichen planus with atrophy.

DR. MARCUS R. CARO: I thought that histologically a better argument could be made for lupus erythematosus than for lichen planus because there were present atrophy of the epidermis and a considerable degree of liquefaction necrosis in the basal layer. The infiltrate contained a number of chromatophores. All these changes are found in lupus erythematosus to a greater extent than in lichen planus.

DR. IRENE NEUHAUSER: Another diagnosis suggested was that of poikiloderma of Civatte. According to Dr. Ormsby's textbook, there are stages of poikiloderma of Civatte in which the histologic changes are indistinguishable from those of lupus erythematosus.

Hairy and Pigmented Nevus. Presented by DR. L. F. WEBER and DR. IRENE NEUHAUSER.

D. S., a woman aged 24, was born with a hairy and pigmented nevus covering a large portion of the medial surface of the left thigh. About three months ago a small mass appeared on the lower portion of the nevus.

Physical examination shows a palm-sized hairy and pigmented nevus on the medial surface of the left thigh. On the surface there is a bluish-reddish tumor, covered with pus, about the size of a walnut. She has discrete and enlarged glands in the left inguinal region.

A histologic section taken from the lesion showed the changes of malignant melanoma.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: This case brings out to me clearly the fact that this type of nevus should be excised by a plastic surgeon who knows how to do it. Some one asked me when I thought it should be done. There is no particular time, of course, but the surgeons prefer to operate when the child is old enough to cooperate.

Linear Eruption. Presented by DR. A. W. STILLIANS.

H. H., a white American youth aged 19, was sent to a sanatorium in New Mexico in February 1944 because of active pulmonary tuberculosis. Within two weeks of his arrival he noticed an eruption on the right forearm, which itched at times. Four months later a red band appeared on the back of the right index finger, causing the nail to split longitudinally and also causing several fissures to appear over the joints. When the patient was seen last December, a brownish red band, 1 cm. in width, extended from the base of the nail along the finger and back of the hand to the wrist. The skin appeared normal for several centimeters proximal to this point, but from there to the elbow the dorsal surface of the forearm was covered with a reticular eruption of scaly yellowish pink macules. This patch faded at the elbow, but about 3 cm. above it was a band about the same width as that on the hand but much less fully developed and light in color, extending 6 cm. After mild irritation, due to a 2 per cent chrysarobin ointment, the patch on the forearm became circinate, and the band above the elbow almost faded out. On the forearm, the radial border of the oval was about 5 mm. in width and elevated, while the ulnar border was flat and ill defined. This is the appearance at the time of presentation, except that there has been an extension of the band on the arm and a small macular eruption in band form has appeared on the right side of the chest near the median line. Recent lesions on the chest and the back are groups of tiny soft flat papules mixed with macules. There is also a faint trace of the macular eruption on the right subscapular region.

The blood counts were normal, and the Wassermann and Kahn reactions were negative. The urine was found normal.

A histologic section taken from the narrow radial border of the lesion on the forearm showed decided edema of the epidermis and the papillary layer of the cutis with great lengthening and in places separation of the basal cells and a considerable infiltrate of round cells about the small blood vessels. At one point parakeratosis was seen, but for the rest of the section the granular layer was present and there were no persistent nuclei in the horny layer.

DISCUSSION

DR. FRANCIS E. SENEAR: The only reason I discuss this case is because several men, seeing the eruption, asked whether it might be an example of lichen striatus. As with any of these linear eruptions, I feel that one has to think of lichen striatus as well as of linear lichen planus, linear nevus and linear psoriasis. This man is beyond the age at which lichen striatus is usually seen. Nearly all my patients were children. Secondly, this eruption has been present for two years. In nearly all my cases of lichen striatus the lesions disappeared spontaneously within a few

years to a few months. This patient has more involvement than has been seen in those cases. He has some irregular bands going across the scapula, and he has some going down across the chest. On the thumb he has a linear patch, and this broadens to form a ring. That ring is a reaction to the use of chrysarobin ointment in this area. Dr. Stillians said that there was a patch of dermatitis. I can see nothing in the clinical picture to suggest psoriasis or lichen planus. Without a histologic examination it would be my feelng that it would be a nevus that developed late in life. I do not think that this eruption is lichen striatus.

DR. A. W. STILLIANS: Nevus was ruled out by the fact that there was definite regression in part of the lesion during the period of observation. I consider the eruption a peculiar example of lichen striatus.

Fixed Eruption Due to a Drug (Sulfathiazole). Presented by DR. M. S. KAGEN (by invitation).

V. B., a man aged 60, entered the hospital on Dec. 11, 1944 for treatment of hypertrophy of the prostate gland. From December 18 on, he was given sulfathiazole, 15 grains (0.97 Gm.) four times a day. After one week of this medication there developed over the face a diffuse redness, which was accompanied with severe smarting sensations. The medication was discontinued, and after a short time the redness and the discomfort subsided almost entirely. He was again given sulfathiazole in a single dose of 15 grains, and the following morning the redness and the discomfort appeared in the same location. Again the drug was discontinued, and the eruption subsided. He was given the same drug last night, with recurrence of the eruption and the discomfort.

DISCUSSION

There was no discussion of this case.

Sickle Cell Ulcers Treated with Red Blood Cells. Presented by DR. MICHAEL EBERT and (by invitation) DR. M. S. KAGEN.

G. H., a Negro man aged 21, had an ulcer on the medial aspect of the left ankle two years ago, followed by a similar ulcer on the medial aspect of the right ankle. When the patient entered the hospital two months ago, the ulcer on the left ankle measured 2½ by 3½ inches (6.4 by 8.9 cm.) and was raised about a quarter of an inch (0.6 cm.) above the level of the skin. Ointment of scarlet red U. S. P. and rest in bed were tried for three weeks, with only slight improvement. Moist red blood cells were applied to the ulcers every morning thereafter, moderate pressure being applied. The ulcers have completely healed for the first time.

The blood count showed 4,200,000 erythrocytes and 7,000 leukocytes. The hemoglobin content was 82 per cent. The urine was normal. The Kahn test was negative.

A moist preparation of the blood showed sickling.

DISCUSSION

There was no discussion of this case.

Granuloma Inguinale. Presented by DR. MICHAEL EBERT and (by invitation) DR. M. S. KAGEN.

O. N., a Negro man aged 44, had an ulcer on the left inguinal area fifteen years ago, which did not increase to more than coin size for five years. During the past ten years the ulceration has extended to the buttocks and about the anus. In 1938 the Kahn test was positive, and for two years thereafter the patient was given antisyphilitic therapy. He has lost considerable weight.

The Frei test elicited no reaction. The Kahn test of the blood was negative. The urine was normal. A smear from the granulation tissue stained with Wright's stain showed Leishmania bodies.

DISCUSSION

DR. THEODORE CORNBLEET: Every once in a while a paper on a new treatment or a revived old treatment of granuloma inguinale appears which stimulates dermatologists toward following the author's recommendations in the treatment of their patients. The results have been poor enough to make me pessimistic. For a while Fuadin seemed to improve the outlook, but it too has not stood the test of time. In some patients there was a temporary improvement with this substance, after which there was a relapse. Resin of podophyllum was irritating and did not do the patients any good. Surgical intervention would seem to offer more when it is feasible. About four or five years ago I sterilized antimony solutions by passing them through a Berkefeld filter. These were no more efficacious than those prepared by heating.

Ainhum. Presented by DR. THEODORE CORNBLEET.

A Negro man aged 47 was born and reared in Louisiana. He has lived in Illinois for twenty years. The left small toe was spontaneously amputated five years ago. The right small toe has been undergoing the present process for two years.

DISCUSSION

There was no discussion of this case.

Neurotic Excoriations. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS and (by invitation) DR. M. S. KAGEN.

S. B., a white girl aged 18, was admitted to the hospital because of an eruption involving the face, the chest and the back and consisting of small bullae and crusts of variable size and configuration but compatible with pemphigus erythematosus. However, histologic examinations of sections on two occasions failed to reveal any pathologic changes.

This girl has congenital syphilis and has had considerable treatment, beginning at the age of 5 years and continuing for about five years.

The urine and the blood count were normal. The Wassermann and Kahn tests were negative. The basal metabolic rate was —6 per cent.

The patient complains of attacks of diarrhea and periodical attacks of palpitation. She suffers from sleeplessness and anxiety, and the pulse rate is rarely under 100 beats per minute.

CLEVELAND DERMATOLOGICAL SOCIETY

Benjamin S. Levine, M.D., *President*

George W. Binkley, *Secretary and Reporter*

Feb. 22, 1945

Lichen Sclerosus et Atrophicus. Presented by DR. W. R. HUBLER.

A. W., a white girl aged 11 years, has had slightly pruritic white spots on the forearms, the shoulders and the feet since May 1944. They appeared suddenly as flat white papules. At no time were they raised or violaceous. There has been no recent change in the eruption.

There are numerous depressed atrophic white areas on the flexor surfaces of the left forearm and the flexor and the extensor surfaces of the right forearm. A few similar areas are present on the shoulders and the trunk. The legs and the dorsa of the feet are also involved. The areas are distributed in a guttate and linear fashion. Many of the lesions have coalesced without losing the outlines of the original papules. Black comedo-like plugs are present in the midportions of most

of the guttate atrophic papules. The vulva, the mouth and the scalp are free of lesions.

The hemogram was normal except for slight hypochromic anemia; the blood sugar level was within normal limits. The Wassermann and Kahn reactions of the blood were negative.

Lichen Sclerosus et Atrophicus. Presented by DR. CLYDE L. CUMMER.

Mrs. T. F., a white woman aged 55, was seen at St. Vincent's Charity Hospital on June 7, 1944 with an eruption which she said had been present for one year.

On the flexor surfaces of the wrists are plaques about the size of a silver dollar, showing thickening of the skin. The surfaces are smooth and shining. The color is that of an oyster shell. At the periphery there is a slight blue coloration. Comedo-like plugs and multiple pinpoint depressions are seen. Atrophy is present. In the other regions the lesions are smaller, those in the crural areas being a few millimeters in diameter only while those on the dorsa of the hands vary from this size to about 1 cm. They also show bluish borders.

The histologic examination was made by Dr. W. P. Jennings and reported as follows: "The section consisted of a portion of skin containing a circumscribed lesion. The lesion was characterized by atrophy of the papillae, increase and condensation of the fibrous tissue in the dermis and almost complete loss of elastic tissue. There was increased vascularization with peripheral cuffing. The vascular reaction was made up of numerous lymphocytes and some fibroblasts. The reaction occurred chiefly at the periphery of the lesion. In the uninvolved portions of the skin, the collagen was loosely arranged and edematous."

After twelve intramuscular injections of bismuth subsalicylate in oil at weekly intervals, there seemed to be some involution with atrophy around the edges of the lesions.

DISCUSSION OF THE TWO PRECEDING CASES

DR. JAMES R. DRIVER: The lesions of A. W. were appearing in scratch marks on the extremities.

DR. CLYDE L. CUMMER: I presented a case of lichen sclerosus et atrophicus before this society on March 25, 1943 (ARCH. DERMAT. & SYPH. **49**:449 [June] 1944). The eruption had been present for five years or longer. The patient was given two courses of bismuth subsalicylate in oil intramuscularly. When the patient was seen for another complaint on Feb. 16, 1945, it was found that the lesions of lichen sclerosus et atrophicus had disappeared completely.

A Case for Diagnosis (Lupus Vulgaris?). Presented by DR. CLYDE L. CUMMER and DR. C. G. LAROCCO.

R. M., a Negro aged 38, was referred to the outpatient department of St. Vincent's Charity Hospital for further treatment. The patient is indefinite as to the length of time "sores" have been present on his body—maybe for several years. He has latent syphilis, for which he received continuous treatment for two years ending March 1944. Since then he has had injections of a bismuth compound in oil at intervals.

On the upper lip and around the nares, at the angles of the jaw and over the penis and the scrotum are pinhead-sized nodules. On the upper lip there is circular grouping around a scar. There is scarring with loss of tissue on the septal side of the left naris. There is no clinical evidence of tuberculosis of the lungs or other tissues.

The Wassermann and Kline reactions of the blood were strongly positive. The hemogram and the urinalysis revealed normal conditions. A roentgenologic examination of the chest showed intensification of the hilar shadows with what probably was a single, slightly enlarged uncalcified node in the left hilus. An examination of the hands and fingers and the feet and toes showed a single punched-out zone of rarefaction in the head of the proximal phalanx of the right fifth toe. A histologic

study revealed that the subcutaneous tissue contained numerous noncaseating tuberculoid lesions. The changes are consistent with tuberculosis or possibly sarcoidosis.

Lupus Vulgaris. Presented by Dr. W. R. Hubler.

Mrs. N. Y., a white woman aged 49, first noticed a small red area "like a little red berry," on each thigh in 1905, when she emigrated from Europe. These have increased slowly in size since then. Following eight roentgen ray treatments, two years ago, ulceration appeared on the right thigh. There has been no other treatment.

An oval, well demarcated red scaly granulomatous plaque, 5 by 7.5 cm., is seen on the anterior portion of each thigh. The middle portions have patchy depigmentation and atrophy. Telangiectasia extends from the centers to beyond the borders of the plaques in some areas. The plaques are raised and red and show deeper soft brownish red macules, 0.5 cm. in size. The remainder of the physical examination revealed no abnormalities.

The hemoglobin content was 13 Gm., and the leukocyte count was 7,100. The blood sugar was within normal limits. The Wassermann and Kahn tests of the blood were negative. An intradermal injection of old tuberculin diluted 1:10,000 gave an indurated papule, 1 cm. in size. A roentgenogram showed that the chest was normal. Biopsy of two plaques revealed essentially the same changes. There were moderate parakeratosis and hyperkeratosis, irregular acanthosis, with intercellular and intracellular edema, and liquefaction degeneration of the basal layer. The entire corium was edematous and contained dilated capillaries. Numerous large nests of epithelioid and lymphocytic cells filled most of the upper two thirds of the dermis surrounding the dermal appendages. They were accompanied with numerous partially formed and complete foreign body and Langerhans' giant cells. A small amount of coagulation necrosis was present in a few of the nodules. In the background the connective tissue was displaced from the nodules and appeared only as thin fibrillar strands between them. No acid-fast bacilli were seen with Ziehl-Neelsen stains.

A salt-free diet was prescribed and has been used by the patient since Dec. 20, 1944. Considerable involution of the plaques can be seen. They are less indurated, slightly smaller and of a lighter color. The apple jelly nodules are probably more apparent because of this.

DISCUSSION OF THE TWO PRECEDING CASES

Dr. Clyde L. Cummer: When Dr. LaRocco and I first saw R. M., we were in doubt as to whether we were dealing with lupus erythematosus or tuberculosis of the skin on account of the infiltration. The appearance was that of Leloir's erythematoid lupus vulgaris. We found a nodule with apple-jelly-like appearance, which was removed for biopsy. It showed the histologic changes associated with tuberculosis. I am satisfied to call this eruption tuberculosis of the skin.

Sarcoidosis. Presented by Dr. E. W. Netherton.

Mrs. M. E., a white woman aged 35, has had brownish purple papules and plaques on the arms and the shoulders since 1941. These have gradually increased in size and number. The cutaneous eruptions were not accompanied with subjective symptoms. The patient's chief complaints were lack of endurance, headache, pain in the chest and a cutaneous eruption which had been present for three years. During this time she felt listless but had had no acute illness. Her tonsils were removed in March 1943, and in September her spleen was removed. An examination of the spleen showed extensive involvement of a sarcoid nature. The Mantoux test done on two previous occasions elicited no significant reaction. Previous roentgenograms showed a normal chest.

There are several brownish red smooth flat doughy epidermal and dermal nodules scattered over the arms and the trunk. There is one small pea-sized

nodule on the right cheek. The nodules vary in size from that of a small lima bean to that of a twenty-five cent piece.

The hemogram showed mild secondary anemia. The Wassermann and Kahn reactions of the blood were negative. A roentgenogram made on Feb. 17, 1945 showed the heart to be normal. There was decided fibrosis in the lower lobe of the right lung, with fibrous infiltration of the upper lobe and the apex. There was a little fibrosis in the lower lobe of the left lung. This was interpreted as pulmonary tuberculosis involving the right apex. Biopsy showed that the epidermis was slightly thinner than normal. The papillary layer of the epidermis was uninvolved. The subpapillary and upper portions of the corium contained numerous circular and fusiform irregular masses, composed principally of large epithelioid cells and surrounded by a narrow dense zone of fibrous connective tissue. There were numerous giant cells of the Langerhans type. There was a small amount of lymphocytic infiltration at the periphery of some of the foci. There were no areas of necrosis.

Sarcoidosis with Ulceration. Presented by DR. W. R. HUBLER.

Mrs. S. W., a white woman aged 37, noted a plaquelike lesion on her right leg five years ago. It was excised. The histologic diagnosis was foreign body reaction. New lesions recurred in the scar and on the adjacent thigh. These crusted at times and often partially disappeared, leaving little scar formation. However, she has not been free of lesions at any time. She has received eleven roentgen ray treatments to the right thigh, with little benefit. Ointments, "iron and arsenic" injections and vitamin A were prescribed, without benefit. She has had psoriasis for twenty years.

On her first visit to the clinic, on May 1, 1944, three granulomatous scarred plaques were present on the anterior part of the right thigh, and faint, light brown plaques, the size of a 25 cent piece, consisting of coalesced glossy pinhead-sized papules, were present on the left shoulder. Since that time, recurrent ulcers have developed on the plaques on the right thigh. These ulcers have been excised, with healing, but eventual recurrence is the rule. In addition, many new lesions have appeared on the body. Recently, the ulcerated areas on the right leg have become painful.

There are three large indurated red-brown plaques on the anterior portions of the right thigh. These present numerous glass pinhead–sized, light red-brown papules along portions of their periphery. On the largest plaque is an irregular ulcer, 5 by 10 cm., with a purulent base. An ulcer, 2 by 3 cm., is present on the medial plaque. Another plaque shows sparse heavy adherent crusting. Numerous sharply demarcated round reddish brown granulomatous plaques, varying from 2 to 6 cm. in diameter, are scattered over the trunk, the neck and the arms. The outlines of the constituent glass pinhead–sized papules are preserved on the smaller lesions. A large lesion on the right side of the trunk is covered with a heavy black crust. There are a few smaller lesions on the vulva. A few circinate lesions of psoriasis are present on the trunk, the scalp and the right elbow.

Repeated hemograms have revealed slight hypochromic anemia. The urine and the blood sugar level were normal. The Wassermann and Kahn reactions of the blood were negative. The tuberculin test, with a 1:10,000 dilution of old tuberculin, resulted in the appearance of an indurated papule, 2 cm. in size. Roentgenograms revealed that the chest and the hands were normal.

The histologic examination of a nonulcerating portion of a plaque on the right leg revealed patchy parakeratosis and irregular acanthosis. Scattered profusely throughout the lower two thirds of the cutis were numerous large mononuclear cells, lymphocytes and eosinophilic leukocytes. Many large multinucleated giant cells of the Langerhans type were scattered throughout the cutis. No acid-fast bacilli were identified with the Ziehl-Neelsen stain. In the deeper portions of the dermis and the subcutaneous tissue there were similar cells, along with circular groups of epithelioid and giant cells around the blood vessels.

Rest, sunlight, supplementary fat-soluble vitamins, neoarsphenamine and injections of solution of sodium arsenate have been prescribed, all without benefit. She also received 1,000,000 units of penicillin; this course of treatment was followed by a severe urticarial eruption lasting from ten to twelve days. Penicillin therapy and a salt-free diet were of no benefit.

Sarcoidosis. Presented by DR. E. W. NETHERTON.

J. M., a man aged 46, came to the Cleveland Clinic on Feb. 1, 1945. His family and past histories were unimportant. His complaint was "lumps" in the skin of the upper extensor surfaces of the arms. These lesions appeared for the first time in 1940. They were small at first but gradually enlarged. New lesions appeared from time to time until, at this examination, the upper lateral and extensor surfaces of the arms, the buttocks and the lower portion of the back were involved. There were no subjective symptoms. The patient's general health has always been good.

There are dull red to reddish brown smooth doughy cutaneous and subcutaneous nodules, ranging in size from that of a hazelnut to that of a small English walnut, on the lateral surfaces of the arms, in the deltoid region and over the upper portion of the back, the lower portion of the back and the sides of the trunk. There are a few lesions on the buttocks. The lesions are poorly defined and not tender. There has been no tendency of the lesions to ulcerate. The larger lesions are covered with small dry adherent scales.

The hemogram showed normal conditions. The Wassermann and Kahn reactions of the blood were negative. An intradermal injection of 0.1 cc. of 1 : 1,000 old tuberculin evoked no significant reaction, but a strongly positive reaction was elicited with old tuberculin diluted 1 : 100.

A roentgenogram of the chest showed extensive fibrosis, particularly in the midlung field. The apexes and the peripheral regions of the lungs are normal. There are a few early calcifications at the upper part of the right hilus and in the midportions of the lungs. A roentgenogram of the hands showed hypertrophic arthritis of the finger joints, particularly severe in the distal joint of the thumb. There is no evidence of rarefaction of the phalanges. The roentgenograms were finally interpreted as evidence of an extensive old bronchitis and hypertrophic arthritis of the hands.

Biopsy of a medium-sized nodule was performed. The histologic section showed slight thinning of the epidermis and slight hyperkeratosis, with slight lymphocytic infiltration of the papillary layer of the corium. Deeper in the corium there were numerous circular irregular granulomatous masses, composed of epithelioid cells, with a rich peripheral infiltration of lymphocytes. There was an occasional giant cell of the Langerhans type but no foci of necrosis.

Sarcoidosis. Presented by DR. E. W. NETHERTON.

Mr. F. B., a railroad fireman aged 35, came to the Cleveland Clinic on Feb. 25, 1943. He complained that the superficial axillary and inguinal lymph nodes had been enlarged for about eighteen months. He had no other complaints, and his general health had been good. His family and past histories were unimportant. Examination showed discrete firm enlarged lymph nodes in the axillary and cervical regions. The epitrochlear nodes were palpable. The spleen was not palpable. The liver was felt on deep inspiration. There were no cutaneous lesions at this time. A provisional clinical diagnosis of Hodgkin's disease was made. Histologic examination of a lymph node removed from the cervical region showed changes consistent with the diagnosis of sarcoidosis.

The patient was again seen on Dec. 15, 1944, because of cutaneous lesions on the forehead, the scalp and the elbows. These lesions have been present for about two years. They consist of oval and round, sharply demarcated, yellowish brown, slightly scaly, infiltrated plaques on the forehead and the scalp, near the hair line of the forehead. The lesions on the forehead are similar to those on the scalp but

differ in that they show atrophy of their central portions. There are split pea-sized pink infiltrated smooth papules on the elbows.

The hemogram revealed no abnormalities. The Wassermann and Kahn reactions of the blood were negative. The Mantoux test showed no reaction to a 1:100 dilution of old tuberculin. A roentgenogram of the chest showed bronchovascular markings, which were unusually prominent throughout the lungs. Scattered along the bronchovascular trunks of the left lobe were several nodules, the largest of which measured 5 cm. in diameter. There was considerable peribronchial infiltration in the lower part of the right lung. The mediastinal lymph nodes were enlarged.

The histologic examination of a small papule removed from the right elbow showed the following conditions: The epidermis was covered with a layer of hyperkeratosis. The granular layer was thickened, and the rete mucosum was thin. There were numerous sharply demarcated nodules composed of epithelioid cells. There were a few giant cells of the Langerhans type in the upper and middle portions of the corium. These nodules were surrounded by narrow zones of collagenous fibers. There were no areas of central necrosis. A few of the foci of infiltration were surrounded by slight amounts of lymphocytic infiltration.

The changes observed in the older lesions of the forehead were somewhat similar. However, the epidermis was thin and was invaded by the cells infiltrating the upper portion of the corium. The infiltration consisted of less well defined single, but more often coalescent, tubercle-like foci of infiltration, consisting of epithelioid giant cells and a moderate number of mononuclear cells, chiefly small lymphocytes. There were some small areas of focal necrosis. No acid-fast bacilli were seen in the Ziehl-Neelsen preparation.

DISCUSSION OF THE FOUR PRECEDING CASES

DR. HAROLD N. COLE: In regard to M. E., I thought that the eruption was a typical example of sarcoidosis with apple-jelly-like nodules which clear in the centers.

DR. W. R. HUBLER: S. W. was presented because of the unusual combination of lesions. The ulcerated areas of sarcoid on the thigh and the tumor-like plaques on the side of the trunk appeared suddenly. The lesions on the legs are of several years' duration. The ulcers appeared about six months ago and have been excised several times. Healing was by secondary intention each time, which was facilitated by penicillin ointment applied locally. It was because of the local infection that 1,000,000 units of penicillin was given intramuscularly over a period of seven days. Each ulcer that was excised and completely healed has recurred in the same area. All the specimens have shown a histologic picture compatible with sarcoid or atypical erythema induratum. Numerous eosinophils have been found in the more recent section. The histologic appearances revealed on biopsy of the tumor-like plaque on the right side of the trunk were identical with those observed in the other biopsies and were not compatible with mycosis fungoides. A lepromin test was positive.

DR. E. W. NETHERTON: S. W. was presented before this society several years ago as having sarcoidosis, but the diagnosis was not accepted. Since she has been under observation the lesions have become disseminated over the body rapidly within the last few months. It is interesting to point out that this patient has a positive reaction to tuberculin in the dilution of 1:10,000.

DR. HAROLD N. COLE: In regard to the cutaneous disease of S. W., clinically the diagnosis should be mycosis fungoides in the fungating stage. The microscopic picture was characteristic of sarcoidosis but I would recommend further study. The patient's clinical appearance is certainly not typical of sarcoidosis.

It is unusual to see so much scaling as in the case of J. M., the man with the lesions on his arm. I would not be able to make a clinical diagnosis. It would be necessary to have a biopsy performed. The patient did not have any changes in his fingers.

DR. E. W. NETHERTON: With reference to J. M., Dr. Cole mentioned that a clinical diagnosis could hardly be made. However, the histologic sections of the specimen removed for biopsy show the typical changes of sarcoid. The man had a negative reaction to old tuberculin in a 1:1,000 dilution.

Amyloidosis of Skin. Presented by DR. JAMES H. BARR JR.

A. M., a white man aged 59, was admitted to the dermatologic outpatient department of University Hospitals on Dec. 13, 1944. At that time he complained of an intensely pruritic eruption of one year's duration on the extensor surfaces of both legs and the left forearm. This eruption first appeared in small groups of lesions above the ankles. The lesions gradually increased in number and extent. The patient has remained in good health throughout this period. The diagnosis of lichen planus was made of a previous cutaneous disease observed at Cleveland City Hospital in 1934.

The general physical examination, including laryngoscopic examination, revealed normal conditions except for the skin and a blood pressure of 175 systolic and 90 diastolic. There are numerous discrete firm hemispheric, seemingly translucent, light brown papules, topped with a hemorrhagic crust, symmetrically located on the extensor surfaces of the lower legs. A tendency toward grouping can be discerned. Similar lesions are manifest on the left wrist.

The hemogram was of interest in that there were 20 per cent normal mature monocytes in the differential count. The results of a complete urinalysis were normal. The result of the Kline exclusion test, the amount of blood urea nitrogen and of plasma proteins, the albumin-globulin ratio, the serum cholesterol level and the blood urea clearances were well within the ranges of normal. A roentgenologic examination showed that the chest was normal. On histologic examination, sections stained with crystal violet showed a hyaline material in the upper part of the dermis, having the staining property of amyloid.

Calamine liniment, containing 0.5 per cent menthol and 10 per cent solution of coal tar, has been prescribed, with satisfactory relief of the pruritus.

DISCUSSION

DR. E. W. NETHERTON: I am sure that Dr. Driver will remember a case that I presented before the society many years ago, as one of a shin guard type of lichen planus. In all probability, it was also a case of amyloidosis, as it resembled the clinical features of the case presented today. The sections showed characteristic amyloid changes.

DR. JAMES R. DRIVER: From the standpoint of therapy I recall a case in which occlusive dressings were used, which kept the patient from scratching. Over a period of a few months the eruption regressed completely.

DR. RUBEN DAVID AZULAY, Rio de Janeiro, Brazil (by invitation): I should like to ask which treatment is regarded as most effective. I can mention one experience I had with the congo red test. The lesions cleared so satisfactorily that the congo red test has been used as therapy in my country.

DR. CHARLES G. LAROCCO: In reply to Dr. Azulay, I recall a case of amyloidosis in which the result of the congo red test was positive for this disease, but subsequent follow-up showed no benefit from the congo red dye.

Pustular Psoriasis; Pustular Bacterid? Presented by DR. E. W. NETHERTON.

Mr. J. O., a clerk aged 31, is presented because of an eruption of one and a half years' duration. The family history is unimportant. His right hand had been amputated because of an accident. The eruption first appeared as a group of "blisters and pustules" on the thenar eminence of the left palm. Six months later, similar lesions developed on the left foot and the inner surface of the left heel. The eruption spread gradually to involve the insteps, the adjacent portions of the soles and the large toes, and more recently lesions have appeared on the

pretibial regions, the knees, the left forearm and the chest. Itching has been present but not troublesome. The eruption failed to respond to roentgen ray therapy and various topical remedies.

There are large well defined red irregular plaques, involving the insteps, the soles, the inner surfaces of the heels and the left palm and wrist. The surfaces of the lesions are in places covered with large gray adherent scales. In other areas there are numerous pinhead-sized tense pustules, while in still other areas the surface of the plaques has a fine granular appearance. There are various-sized erythematous scaly plaques of the psoriasiform type on the extensor surfaces of the legs, the midportion of the chest, the forearms and the knees. The scalp is not involved. The large toe nails are rough, thickened and friable, and the nail fold is involved by a scaly erythematous eruption, similar to that involving the instep.

The hemogram was normal. The Wassermann and Kahn reactions of the blood were negative. Material removed from the thickened nails and from the hands and the soles for potassium hydroxide preparation did not reveal hyphae.

A histologic study of tissue removed from a psoriasiform lesion of the lower portion of the right leg showed a change which involved chiefly the epidermis. The surface of the epidermis was covered with a layer of hyperkeratosis and parakeratosis. There was acanthosis. The papillae varied in length and width, and some were covered with a thin layer of epidermis. The basal cell layer was intact. There were edema, vascular dilatation and moderate perivascular lymphocytic infiltration in the papillae and the subpapillary portion of the corium. There was no typical Monro abscess. However, there were small collections of leukocytes in some of the hyperkeratotic and parakeratotic scales.

DISCUSSION

DR. HAROLD N. COLE: All dermatologists see recalcitrant pustular eruptions of the palms and the soles. It is rare to see one for which the term "pustular psoriasis" may be used. The patient has typical pustular areas on the palms and the soles, along with lesions over the sternum, that are suggestive of a psoriatic process.

DR. E. W. NETHERTON: Dr. Cole has mentioned the main reason for showing this patient. All the members have seen chronic scaly pustular erythematous lesions on the palms and the soles such as this patient presented, and have had considerable difficulty in arriving at the proper diagnosis, the diagnosis often resting between bacterid and pustular psoriasis. In this case, however, there are definite, rather typical lesions of psoriasis on the knees and the legs. The histologic study of biopsy material shows changes characteristic of psoriasis.

Trophic Ulcers Following Nerve Resection. Presented by DR. CLYDE L. CUMMER.

M. J. F., a white man aged 63, was operated on in February 1932 for tic douloureux of the left side of the face; presumably a resection of the gasserian ganglion was done. He had no difficulty with the skin of the left side of the face and the scalp for almost ten years, although there was complete loss of sensation in this area. There were trophic ulcers of the cornea of the left eye. This resulted in scarring and impairment in vision.

On Sept. 7, 1944 he presented deep irregular scars on the left side of the face. On the upper left eyelid was a clean sluggish deep ulcer, almost covering the entire lid. There was a similar ulcer on the left side of the forehead and numerous areas resembling excoriations on the left vertex.

Ointment of scarlet red N. F. was prescribed, with great improvement in the ulcers of the skin.

DISCUSSION

DR. HAROLD N. COLE: The patient gives a typical history of neurotic excoriations. Granted, there is an area of trophic change, but, in addition, he has been picking the areas.

Book Reviews

Skin Diseases in Children. By George M. MacKee, M.D., and Anthony C. Cipollaro, M.D. Second edition. Price, $7.50. Pp. 448, with 225 black and white photos. New York: Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 1946.

This excellent book in its second edition has been greatly enlarged and completely rewritten. It contains twenty-two chapters, including four new ones on dermatologic allergy, the exanthemas, congenital anomalies and congenital syphilis by other writers. No attempt at scientific classification has been made, the subjects being discussed partly on etiologic and partly on pathologic grounds and partly on the basis of clinical similarity.

The book is written mainly for the general practitioner, though much information of value to the dermatologist is given. Most of the treatment suggested is based on the wide experience of the authors. An adequate bibliography is included at the end of each chapter.

One of the most valuable features of the book is the two hundred and twenty-five black and white clinical photographs. They are unusually good, well chosen and, owing to the fairly heavy glazed paper used in the entire book, splendidly reproduced. The frontispiece, consisting of four colored pictures, does not compare in value with the black and white illustrations.

The authors have carefully followed the Standard Nomenclature of Disease, though in 2 instances slips were made, one being the use of "lymphogranuloma inguinale" in place of "venereal lymphogranuloma," and the other, a minor but common mistake, "nevus unius lateralis" instead of "nevus unius lateris."

The book is clearly written and contains up-to-date information which makes it a most valuable treatise for the dermatologist and general practitioner alike.

Corky the Killer: A Story of Syphilis. By Harry A. Wilmer, M.D. Introduction by Paul A. O'Leary, M.D., with forewords by Joseph E. Moore, M.D. and by Kendall Emerson, M.D. Price, $1. Pp. 66. New York: American Social Hygiene Association, Inc., 1945.

The author has told the story of syphilis to the layman in a most interesting and graphic manner. The villain in the story, called Corky, represents a spiral-shaped Treponema pallidum, who with his millions of comrades attempts to destroy every part of the human body. The illustrations by the author are unique and graphically show the attacks of the spirochete on various organs. Each page gives the story of Corky's machinations in understandable language. At the bottom of each page the scientific facts are explained in language any layman can understand. A book that is limited to the scientific story would not be read by as many laymen as one that is combined with the bizarre drawings of Corky and his experiences. This book should have a large sale and is a distinct contribution to the fight against syphilis.

News and Comment

Section on Dermatology and Syphilology, American Medical Association, Centennial Anniversary Meeting.—All who desire to read papers before the Section on Dermatology and Syphilology at the Centennial Anniversary meeting of the American Medical Association in Atlantic City, N. J., in June 1947 will please write to the Secretary. There will be fewer positions available for members on account of invitations to a few foreign guest speakers. Applications should be addressed to Clinton W. Lane, M.D., Secretary of the Section on Dermatology and Syphilology, Metropolitan Building, St. Louis 3, Mo.